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No. 96- OFFICE OF THE CLERK

IN THE

Supreme Court of the United States

OCTOBER TERM, 1996

ORGANON INC.,

Petitioner,

v.

DAVID A. KESSLER, M.D.,
Commissioner of Food and Drugs,
BRUCE LEHMAN, Assistant Secretary of Commerce and
Commissioner of Patents and Trademarks, and
GENERIC PHARMACEUTICAL INDUSTRY ASSOCIATION,

Respondents.

On Petition for a Writ of Certiorari to the United States Court of Appeals for the Federal Circuit

PETITION FOR WRIT OF CERTIORARI

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QUESTIONS PRESENTED

1. Whether a patent that is in force on June 8, 1995 due to a Hatch-Waxman restoration extension under 35 U.S.C. § 156(c) is a patent "in force" within the meaning of the Uruguay Round Agreements Act, as codified at 35 U.S.C. § 154(c), and therefore entitled to a recalculated 20-years-from-application patent term.

2. Whether the United States Food and Drug Administration violated the Administrative Procedure Act by creating three new substantive rules without providing the requisite notice-and-comment period.

RULE 29.6 STATEMENT

This Petition is filed on behalf of Organon Inc. The parent company of Organon Inc. is Akzo Nobel. Organon Inc. does not have any nonwholly owned subsidiaries. The other parties to the proceedings in the United States Court of Appeals for the Federal Circuit were: Merck & Co., Inc. and MSD Technology, L.P.; Schering Corporation; Bracco Diagnostics Inc. and Bracco International B.V.; Hoffmann-LaRoche Inc. and Syntex (U.S.A.) Inc.; David A. Kessler, M.D.; Bruce A. Lehman; and the Generic Pharmaceutical Industry Association.

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The opinion of the United States Court of Appeals for the Federal Circuit (the "Federal Circuit") in this matter is reported at 80 F.3d 1543 (Fed. Cir. 1996). (App. 1a-23a). The opinion of the United States District Court for the Eastern District of Virginia (the "District Court") in *Merck & Co. v. Kessler* is reported at 903 F. Supp. 964 (E.D. Va. 1995). (App. 28a-39a). The District Court's decision in the companion case to *Merck & Co. v. Kessler* filed by Petitioner Organon Inc. ("Organon") was filed in Case No. 95-1380-A, but is not officially reported. (App. 24a-27a).

The "Final Determination" of the United States Patent and Trademark Office (the "PTO") on the issue in this case is published at 60 Federal Register 30069 (June 7, 1995). (App. 56a-66a). The United States Food and Drug Administration (the "FDA") adopted the PTO's Final Determination on this issue in its "Notice" published at 60 Federal Register 37652 (July 21, 1995). (App. 74a-79a).

JURISDICTION

The Federal Circuit's judgment in this case was entered on April 4, 1996. Three combined petitions for rehearing and suggestions for rehearing *in banc*, including one filed by Organon, were denied by the Federal Circuit on July 12, 1996. This Court has appellate jurisdiction to review the decision of the Federal Circuit pursuant to 28 U.S.C. § 1254(1).

TREATIES AND STATUTES AT ISSUE

Portions of the Uruguay Round Agreements Act (the "URAA"), Pub. L. No. 103-465, 108 Stat. 4983-85, 4990 (1994), are at issue in this case. Specifically, those portions of the URAA codified at 35 U.S.C. § 154 are directly at issue. (App. 95a-98a). The Hatch-Waxman Act, as codified at 35 U.S.C. § 156, is also directly at issue. (App. 99a-118a). Organon also alleges herein that portions of the Administrative Procedure Act, as codified at 5 U.S.C. § 553, have been violated in this case. (App. 119a-121a). A number of other statutes and regulations are also involved in this case, including 21 U.S.C. § 355 (App. 122a-160a); 21 C.F.R. § 314.53 (App. 190a-197a); 21 C.F.R. § 314.50 (App. 161a-189a); 21 C.F.R. § 314.94 (App. 198a-215a), the relevant text of which are set out in the appendix hereto.

STATEMENT OF THE CASE

Organon filed its Complaint in this matter in the District Court on October 2, 1995, relying on 28 U.S.C. §§ 1331, 1332, 1338, and 2201-2202 as bases for federal jurisdiction. Organon filed suit because it was being denied its statutory right to a 20-years-from-application patent term expiration date under the URAA by the interpretation of that statute issued by the Commissioners of the PTO and the FDA. The patent with which Organon is concerned in this case is United States Patent No. 3,927,046 ("the '046 patent"). The '046 patent protects Desogestrel, an active ingredient in the Desogen® prescription birth control pills which Organon markets as the holder of a license for the '046 patent. At the time that Organon filed suit in the District Court, a number of other pharmaceutical companies had already filed suit in

that court raising similar issues regarding the propriety of a patent receiving both a Hatch-Waxman restoration extension and a 20-years-from-application patent term expiration date under the URAA.

On October 16, 1995, the District Court consolidated all of the cases then pending on this issue, except the *Organon* case. The case filed by Merck & Co., Inc. was designated the lead case and the consolidated actions were thereafter referred to as *Merck & Co. v. Kessler*. On that same date, the District Court also entered summary judgment in favor of the plaintiff pharmaceutical companies in that consolidated action, holding that the plaintiffs were statutorily entitled to receive the benefits of *both* their Hatch-Waxman restoration extensions and a 20-years-from-application patent term expiration date under the URAA. *Merck & Co. v. Kessler*, 903 F. Supp. 964, 966 (E.D. Va. 1995). (App. 32a-35a).

On October 23, 1995, Organon also moved for summary judgment in its case. Organon argued that it was entitled to judgment as a matter of law based on the District Court's decision in the earlier consolidated cases. Organon, however, also timely raised in the District Court (thereby preserving for appellate review) additional arguments which mandated that summary judgment be entered in Organon's favor.

On November 9, 1995, the District Court awarded Organon summary judgment "for the same reasons" set forth in the October 16, 1995 Opinion and Order in *Merck & Co. v. Kessler*, 903 F. Supp. 964 (E.D. Va. 1995). (App. 24a). The District Court also ordered "the same injunctive and declaratory relief" which was "accorded to the plaintiffs in that [earlier] action." *Id.* On November

21, 1995, the Commissioners of the PTO and the FDA (collectively, the "Federal Appellants") filed their Notice of Appeal from the District Court's decision in the *Organon* case. The Federal Appellants, as well as the intervenor Generic Pharmaceutical Industry Association ("GPIA"), also timely appealed the District Court's decision in *Merck & Co. v. Kessler* to the Federal Circuit pursuant to 28 U.S.C. § 1295(a)(1). The two appeals were subsequently consolidated by order of the Federal Circuit.

In its decision in this case, the Federal Circuit first created a factual distinction which classified the various patents at issue into two separate groups -- those which had utilized their Hatch-Waxman restoration extension prior to June 8, 1995, and those which had not utilized their Hatch-Waxman restoration extension prior to that date. Based on this previously immaterial factual distinction, the Federal Circuit then

> conclude[d] that pre-June 8, 1995, patents are entitled to add on the restoration extension to a 20-year from filing term regardless of when such extension is granted *except for those patents kept in force on June 8, 1995, only because of a restoration extension.*

Merck & Co. v. Kessler, 80 F.3d 1543, 1550 (Fed. Cir. 1996) (emphasis added). (App. 15a). In other words, the Federal Circuit held that patents in force on June 8, 1995 solely due to their Hatch-Waxman restoration extension were not entitled to receive the benefits of both their Hatch-Waxman restoration extension and the 20-years-from-application patent term expiration date mandated by

the URAA. Organon now seeks Supreme Court review of that decision.

REASONS FOR GRANTING THE PETITION

As stated *supra*, there are two statutes directly at issue in this case. The first statute results from President Clinton's December 8, 1994 decision to sign into law the URAA, which implements the General Agreement on Tariffs and Trade ("GATT") and the accompanying Agreement on Trade-Related Aspects of Intellectual Property Law ("TRIPs"). The URAA and TRIPs were enacted to bring the United States into line with the patent protections provided by the other signatory countries to this agreement, thereby affording universal intellectual property protection to all member countries. By its terms, the URAA amended the federal Patent Act.

The Hatch-Waxman Act is the second statute at issue. The Hatch-Waxman Act was passed 10 years before the URAA (in 1984) and struck a delicate balance between promoting cheaper, generic versions of pioneer drugs and rewarding pioneer drug companies for expending the time and money necessary to develop those drugs in the first instance. On one hand, the Hatch-Waxman Act provided for restoration extensions to the existing terms of patents which have lost some of their effective patent life while awaiting FDA approval. 35 U.S.C. § 156 (Supp. 1996). (App. 99a-118a). Therefore, part of the purpose of the Hatch-Waxman Act was to "ameliorate the loss incurred when patent terms tick away while the patented product is awaiting regulatory approval for marketing [by the FDA]," *Unimed, Inc. v. Quigg*, 888 F.2d 826, 829 (Fed. Cir. 1989), and therefore "encourage[] more research on new drug compounds." 130 Cong. Rec. 15847 (1984) (statement by

Sen. Hatch). On the other hand, the Hatch-Waxman Act also promotes the availability of generic versions of pioneer drugs by offering generic drug companies the opportunity to obtain FDA approval of generic copies of a pioneer drug through a streamlined procedure simply by filing an Abbreviated New Drug Application ("ANDA"). 21 U.S.C. § 355(j) (Supp. 1996). (App. 140a-158a). Through the ANDA process, the generic drug company can inexpensively manufacture its product by simply relying on the research already done by the pioneer drug company as evidence that the generic copy of the pioneer drug is also safe and effective. 21 U.S.C. § 355(j)(2)(A) (Supp. 1996). (App. 140a-143a).

The issue in this case is one of first impression in which the important federal policies promoted by both the URAA and the Hatch-Waxman Act intersect and have been seriously jeopardized. Far from promoting the stated objectives of both the URAA and the Hatch-Waxman Act, the Federal Circuit's decision in this case undermines both of those significant federal policies. The Federal Circuit's decision strips Organon of its statutory right to a 20-years-from-application patent term expiration date under the URAA, while simultaneously violating the United States's promise to other URAA member nations that it would thereafter provide 20-years-from-application patent terms for U.S. patents. This Court should rectify the serious mistake of law made by the Federal Circuit.

I. THE FEDERAL CIRCUIT'S DECISION IS INTERNALLY INCONSISTENT AND DIRECTLY CONTRARY TO THE MANDATORY AND UNQUALIFIED LANGUAGE OF 35 U.S.C. § 154(C)(1).

Before the URAA and TRIPs were enacted on December 8, 1994, Section 154 of the federal Patent Act set the term for all patents at 17 years *from the date the patent issued.* 35 U.S.C. § 154 (1984) (amended 1994). Under TRIPs, the United States was obligated to provide all patents with a term of at least 20 years from the date of application. *See* TRIPs Article 33 ("The term of protection available shall not end before the expiration of a period of twenty years counted from the filing date."). Therefore, Congress amended Section 154 to provide for newly created patent terms under the URAA as follows:

> Subject to the payment of fees under this title, such grant shall be for a term beginning on the date on which the patent issues and *ending 20 years from the date on which the application for the patent was filed in the United States* . . . .

35 U.S.C. § 154(a)(2) (Supp. 1996) (emphasis added). (App. 95a). Consequently, every patent for which an application is filed after the effective date of the URAA will now be granted a 20-years-from-application patent term expiration date by the PTO.

Congress also provided transitional provisions in the newly amended Section 154 which addressed patents already in force on the effective date of the URAA (*i.e.*, June 8, 1995) and patents which had been applied for --

but not issued -- prior to this date. For these patents, amended Section 154 provides that:

> The term of a patent that is *in force* on or that results from an application filed before [June 8, 1995] *shall be the greater of the 20-year [from application] term as provided in subsection (a), or 17 years from grant,* subject to any terminal disclaimers.

35 U.S.C. § 154(c)(1) (Supp. 1996) (emphasis added). (App. 97a-98a). In other words, patents already "in force" on June 8, 1995 automatically received, by operation of law, either a 20-years-from-application patent term or a 17-years-from-grant patent term, whichever was longer. *Id.*

Congress's use of the term "shall" in amended Section 154(c)(1) unmistakably indicates its intention that there be a mandatory requirement that these patent term expiration dates be recalculated as 20-years-from-application or 17-years-from-grant, whichever is longer. *Southern Ry. Co. v. Seaboard Allied Milling Corp.*, 442 U.S. 444, 456 (1979). There is no room for any other interpretation of the statute. In its decision in this case, however, the Federal Circuit has unlawfully rewritten the statute by engrafting the following underscored language:

> The term of a patent that is in force on or that results from an application filed before [June 8, 1995] shall be the greater of the 20-year [from application] term as provided in subsection (a), or 17 years from grant, subject to any terminal disclaimers, <u>unless the patent is in force on June 8, 1995 solely</u>

due to a Hatch-Waxman restoration
extension pursuant to 35 U.S.C. § 156.

35 U.S.C. § 154(c)(1) (Supp. 1996) (as modified by underscored language). Notwithstanding the Federal Circuit's strained interpretation of this statute, Congress never provided for the exception created by the Federal Circuit. The Federal Circuit has rewritten the statute.

In fact, the only criterion that Congress imposed on these transitional patents in order for them to receive "the greater" of a 20-years-from-application patent term or a 17-years-from-grant patent term is that they be "in force" on June 8, 1995 (or have an application filed prior to that date). 35 U.S.C. § 154(c)(1) (Supp. 1996). (App. 97a-98a). In its own decision in this case, the Federal Circuit recognized that Organon's '046 patent was a patent "***in force on June 8, 1995***." *Merck & Co. v. Kessler*, 80 F.3d 1543, 1546, 1548 (Fed. Cir. 1996) (emphasis added). (App. 3a-4a, 9a). Consequently, the text of the Federal Circuit's decision is internally inconsistent with its stated holding and plainly at odds with the mandatory and unqualified language of the statute passed by Congress.

Moreover, the Federal Circuit ignored a well-established rule of statutory construction in rendering this decision. This Court has long held that courts should "presume that Congress is knowledgeable about existing law pertinent to the legislation it enacts." *Goodyear Atomic Corp. v. Miller*, 486 U.S. 174, 185 (1988); *see also Miles v. Apex Marine Corp.*, 498 U.S. 19, 32 (1990). Because "it is proper to consider that Congress acts with knowledge of existing law, . . . 'absent a clear manifestation of contrary intent, a newly-enacted or revised statute is presumed to be harmonious with existing law and

its judicial construction.'" *Estate of Wood v. Commissioner*, 909 F.2d 1155, 1160 (8th Cir. 1990) (*quoting Johnson v. First Nat'l Bank*, 719 F.2d 270, 277 (8th Cir. 1983), *cert. denied*, 465 U.S. 1012 (1984)).

With one exception that does not support the Federal Circuit's decision in this case, the URAA did not alter the existing Hatch-Waxman Act. Therefore, because the Hatch-Waxman Act had been enacted nearly ten years prior to the URAA, the Federal Circuit should have presumed that Congress was aware of the existence of the Hatch-Waxman Act when it enacted the URAA. *Id.* The Federal Circuit should have also presumed that Congress was aware that some patents would be "in force" on June 8, 1995 solely due to their Hatch-Waxman extensions. *Id.*; *see also Roche Prods., Inc. v. Bolar Pharmaceutical Co.*, 733 F.2d 858, 864 (Fed. Cir.), *cert. denied*, 469 U.S. 856 (1984). As a result, under well-established principles of statutory construction, the Federal Circuit *should* have also concluded that the URAA and the Hatch-Waxman Act were "harmonious," and that, as the PTO originally concluded, all patents "in force" on June 8, 1995 were entitled to receive the benefits of both a Hatch-Waxman restoration extension and a 20-years-from-application URAA patent term expiration date under the URAA.

The Federal Circuit was also mistaken in its conclusion that application of a 20-years-from-application patent term expiration date under the URAA to a patent which was in force on June 8, 1995 solely due to the existence of a Hatch-Waxman restoration extension would somehow violate the prohibition in 35 U.S.C. § 156(a)(2) against so-called "double extensions." *Merck & Co. v. Kessler*, 80 F.3d 1543, 1550 (Fed. Cir. 1996). (App. 15a-23a). The one amendment which the URAA made to the

Hatch-Waxman Act (as codified at 35 U.S.C. § 156(a)(2)) was to add the language underscored below to 35 U.S.C. § 156(a)(2):

> The term of a patent which claims a product, a method of using a product, or a method of manufacturing a product shall be extended in accordance with this section from the original expiration date of the patent if . . . the term of the patent has never been extended <u>under subsection (e)(1) of this section</u> . . . .

35 U.S.C. § 156(a)(2) (Supp. 1996). (App. 99a). Subsection (e)(1) governs the award of Hatch-Waxman restoration extensions. Thus, this language was added to the statute to make it clear that only one Hatch-Waxman restoration extension per patent was permitted. In this case, Organon's '046 patent has not received two Hatch-Waxman restoration extensions -- rather, the '046 patent has received one Hatch-Waxman restoration extension and one recalculated patent term expiration date under the URAA. There is absolutely no language anywhere in the URAA or the Hatch-Waxman Act which prohibits Organon from enjoying the benefits of both of these statutes.

In fact, even the literal language of Section 156(a)(2), upon which the Federal Circuit relied in its decision, does not support its conclusion in this case that patents which have received -- but not utilized -- a Hatch-Waxman restoration extension prior to June 8, 1995 are entitled to a 20-years-from-application patent term expiration date under the URAA, but patents which have received -- ***and*** utilized -- a Hatch-Waxman restoration extension prior to June 8, 1995 are ***not*** entitled to a 20-

years-from-application patent term expiration date under the URAA. *Merck & Co. v. Kessler*, 80 F.3d 1543, 1550 (Fed. Cir. 1996). (App. 15a-23a). Both of these groups of patents have been "extended" within the meaning of Section 156(a)(2) because the Hatch-Waxman extension which the former group received was actually added to its patent term on the effective date of the granting of the extension. *See* 35 U.S.C. § 156(e)(1) (Supp. 1996) ("Such [restoration extension] certificate shall be recorded in the official file of the patent and shall be considered as part of the original patent."). (App. 110a). Consequently, there is no basis in the language of the statute to discriminate against patents which have utilized their Hatch-Waxman extension prior to June 8, 1995. Either both groups of patents violate Section 156(a)(2), or neither does. The Federal Circuit's decision is therefore inconsistent in this respect also.

For all of the foregoing reasons, this Court should not allow the decision of the Federal Circuit to stand. The Federal Circuit's decision has completely upset the delicate balance previously struck by the Hatch-Waxman Act. In addition, the reasoning employed by the Federal Circuit is directly at odds with numerous decisions by this Court. A writ of *certiorari* should issue to the Court of Appeals for the Federal Circuit to correct these serious errors of law.

II. THE JULY 21, 1995 FDA NOTICE WAS NOT PROMULGATED IN COMPLIANCE WITH THE APA.

Notwithstanding the important questions of federal law and policy in this case that need to be decided by this Court, there is also a significant question of federal law pertaining to the ability of an administrative agency to

circumvent the Administrative Procedure Act ("APA"). During the course of this case, the FDA has completely flouted key provisions of the APA. The APA was designed to bring structure and order to agency rulemaking activities. Unless the FDA's transgressions are corrected by this Court, fundamental principles of the APA will undoubtedly be eroded.

On January 17, 1995, while the issue in this case was still being addressed at the agency level, the ***PTO*** requested comments on, and noticed a public hearing regarding, the effect that the URAA would have on patents which had previously received extensions under the Hatch-Waxman Act. *See* 60 Fed. Reg. 3398 (Jan. 17, 1995). (App. 42a-51a). At that time, the PTO indicated its initial assumption that the URAA "extension is separate from, and in addition to, the patent term extension available under [the Hatch-Waxman Act]." *Id.* Similarly, on March 27, 1995, after receiving comments from interested parties, the PTO published in the Federal Register its "Proposed Determination" on this issue, in which it stated its intention to consider

> [a] patent that would have expired under the original 17-year patent term before June 8, 1995, but that has received a patent term extension for a period beyond June 8, 1995, [as] a patent "in force" on June 8, 1995 . . . [within the meaning of the URAA].

60 Fed. Reg. 15748, 15749 (Mar. 27, 1995). (App. 54a).

On June 7, 1995, however, the PTO did an about face and completely reversed its prior position regarding the manner in which patent expiration dates would be

calculated under the URAA and the Hatch-Waxman Act. On that date, the PTO published in the Federal Register its "Final Determination" on this issue, in which it indicated that it would calculate the patent term expiration date for patents which were in force on June 8, 1995 and had already received a Hatch-Waxman restoration extension as *either* (a) 17 years from the date of the granting of the patent application plus the Hatch-Waxman restoration extension, or (b) 20 years from the date of filing the application, whichever was longer. *See* 60 Fed. Reg. 30069 (June 7, 1995). (App. 56a-66a). In other words, the PTO now took the position that a Hatch-Waxman restoration extension could not be added to the 20-years-from-application patent term mandated by the URAA.

On July 21, 1995, the FDA announced in the Federal Register its newly-fabricated "position" that it would "not publish dates that the NDA . . . applicant states are not calculated in accordance with the [PTO's] June 7, 1995 [final] determination." 60 Fed. Reg. 37652 (July 21, 1995) (the "July 21, 1995 FDA Notice"). (App. 74a). The FDA also indicated that the procedures set out in 21 C.F.R. § 314.53(f), which had previously been the subject of a notice-and-comment rulemaking, would be "modified" as a result of its new "position." *Id.* (App. 77a-78a). Without conducting its own rulemaking, as required by the APA, or providing any notice and/or comment period to Organon and others whose products are subject to FDA regulation, the FDA simply adopted the PTO's "Final Determination" as its own interpretation of the URAA's application to patents under Hatch-Waxman restoration extensions on June 8, 1995. In so doing, the FDA created ***three new substantive rules*** without adhering to even the most minimal of the fundamental principles required by the APA.

A. The FDA Impermissibly Promulgated A New Rule Regarding The FDA's Role In Publishing Patent Term Expiration Dates Without Notice-And-Comment Rulemaking.

Prior to July 21, 1995, the FDA had been very consistent and very clear that it had no discretion to refuse to publish a patent term expiration date provided by a New Drug Application ("NDA") holder or applicant. The FDA regulations, promulgated pursuant to notice-and-comment rulemaking, provide that the "FDA ***will publish*** in the [Orange Book][1] the patent number and expiration date of each patent that is required to be, and is, submitted to FDA by an [NDA] applicant." 21 C.F.R. § 314.53(e) (1995) (emphasis added). (App. 195a). The regulations are mandatory; no discretion is left to the FDA. The FDA's statutory directive is also mandatory with respect to the patent information that has been provided by the NDA applicant -- upon approval of the application, the FDA "***shall publish***" this patent information and make it available to interested parties. 21 U.S.C. §§ 355(b)(1), (c)(2) (Supp. 1996) (emphasis added). (App. 123a). This "ministerial role" was reiterated as recently as May 25, 1995 in the FDA's response to a Citizen Petition filed by Glaxo Pharmaceuticals, Inc. ("Glaxo"). In that response, the FDA insisted that the agency acts in a "solely

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[1] The official title of the "Orange Book" is Approved Drug Products With Therapeutic Equivalence Evaluations (15th ed. 1995), which contains the patent information provided by NDA applicants, such as patent numbers and corresponding expiration dates. It is commonly referred to as the Orange Book for its orange cover.

ministerial capacity" when it accepts and publishes patent information from an NDA holder or applicant. *See* Record in the Federal Circuit at 355. [2/]

Nevertheless, in its July 21, 1995 Notice, the FDA completely reversed its previous stance that its duties with respect to the publication of patent expiration dates in the Orange Book were purely ministerial. In that Notice, the FDA announced its new "position" that it would "***not publish*** dates that the NDA . . . applicant states are not calculated in accordance with the [PTO's] June 7, 1995 [final] determination." 60 Fed. Reg. 37652 (July 21, 1995) (emphasis added). (App. 74a).

This "position" was a new rule by the FDA. A new substantive rule is created whenever an agency takes any action which "repudiates or is irreconcilable with" a prior substantive rule. *American Mining Congress v. MSHA*, 995 F.2d 1106, 1109 (D.C. Cir. 1993) (*quoting National Family Planning & Reproductive Health Ass'n v. Sullivan*, 979 F.2d 227, 235 (D.C. Cir. 1992)). The July 21, 1995 FDA Notice repudiated the provisions of 21 C.F.R. § 314.53(e) (1995), which ***required*** the FDA to publish ***all*** patent term expiration dates provided by NDA holders or applicants. The rule contained within the July 21, 1995 FDA Notice was not promulgated pursuant to the notice-

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[2/] On June 8, 1995, the FDA publicized its response to Glaxo's Citizen Petition in the Federal Register by announcing that it had responded to the Citizen Petition and noting that copies of its response were available from the FDA's Freedom of Information Staff. 60 Fed. Reg. 30309 (June 8, 1995). (App. 67a-73a).

and-comment requirements of Section 553 of the APA, 5 U.S.C. § 553 (1996), and is therefore void.[3/]

B. The FDA Impermissibly Promulgated A New Rule Regarding The Procedure For Challenging Patent Term Expiration Dates Without Notice-And-Comment Rulemaking.

The FDA also promulgated a ***second*** new substantive rule in its July 21, 1995 Notice, and again disregarded the notice-and-comment requirements of Section 553 of the APA, 5 U.S.C. § 553. The method for challenging a patent term expiration date is governed by 21 C.F.R. § 314.53(f) (1995). Under that provision, if an ANDA applicant disputes the accuracy of the patent expiration date listed in the Orange Book, it may seek confirmation of that information through the FDA, which will then request confirmation of the patent expiration date from the NDA holder. 21 C.F.R. §§ 314.53(f) (App. 196a-197a), 314.50(i)(5) (App. 183a-184a), 314.94(a)(12)(vii) (1995) (App. 210a). However, according to the FDA's regulations, "[u]nless the [NDA] holder withdraws or amends its patent information in response to FDA's request [for confirmation], ***the agency will not change the patent information in the list.***" Id. at § 314.53(f) (1995) (emphasis added). (App. 196a).

[3/] In addition to violating the APA, the FDA's blatant disregard of its own procedures is a due process violation. *Berends v. Butz*, 357 F. Supp. 143, 151 (D. Minn. 1973) ("[t]he failure of an administrative agency to follow its own established procedures constitutes a violation of procedural due process").

Nevertheless, in its July 21, 1995 Notice, the FDA indicated that the procedures set out in 21 C.F.R. § 314.53(f) (and quoted immediately above) would be "modified" to support its new "position," described *supra*. 60 Fed. Reg. 37652 (July 21, 1995). Under the FDA's new "modification," after July 21, 1995, if an NDA holder does not respond to the FDA's request for confirmation of the accuracy of its patent expiration date within 30 days, and if the NDA holder does not notify the FDA that the patent expiration date is consistent with the PTO's June 7, 1995 interpretation of the URAA, the FDA "***will not continue to publish the challenged date.***" *Id.* (emphasis added). (App. 78a). This is a significant change from the prior rule because, beginning on July 21, 1995, if the NDA holder fails to respond to the FDA's inquiry, it would lose its Hatch-Waxman restoration extension. This new rule therefore repudiates a previous rule which was issued following notice-and-comment rulemaking and, as such, the APA requires that it be subject to those same procedures. *American Mining Congress*, 995 F.2d at 1109. The rule is therefore void until the FDA completes a notice-and-comment rulemaking proceeding for this rule.

C. The July 21, 1995 FDA Notice Is Itself A Rule Which Impermissibly Interprets The Effect That The URAA Has On The Hatch-Waxman Act.

In its July 21, 1995 Notice, the FDA also adopted the PTO's Final Determination as its own rule interpreting the effect that the URAA has on the Hatch-Waxman Act. In so doing, the FDA created a ***third*** new substantive rule without complying with the procedures provided for in the APA. Section 553 of the APA states:

> After notice required by this section, ***the agency*** shall give interested persons an opportunity to participate in the rule making through submission of written data, views, or arguments with or without opportunity for oral presentation. After consideration of the relevant matter presented, ***the agency*** shall incorporate in the rules adopted a concise general statement of their basis and purpose.

5 U.S.C. § 553(c) (1996) (emphasis added). (App. 120a). It is clear from the statute that "the agency" which is promulgating the rule is also "the agency" that must provide the public with an opportunity to comment. No other reading of the statute makes sense. In other words, there is no language in the statute which permits the ***FDA***, as the rulemaking agency, to rely on the notice-and-comment proceeding performed by the ***PTO***, precisely because they are independent federal agencies. *Cf. Morgan v. United States*, 304 U.S. 1 (1938) (holding that due process was not satisfied because, *inter alia*, the Secretary of Agriculture made his decision based in part on proposed

findings of employees of the Bureau of Animal Industry). An independent notice-and-comment rulemaking is particularly important in a situation such as this where the FDA has administrative responsibility for regulating pharmaceuticals, such as Organon's Desogen® birth control pills. If the FDA wanted to adopt the PTO's Final Determination as its own rule, it was still required to perform ***its own notice-and-comment rulemaking proceeding*** before doing so. The FDA's adoption, therefore, of the PTO's Final Determination is null and void until the FDA conducts its own notice-and-comment rulemaking proceeding.

In summary, each of the ***three new substantive rules*** described *supra* clearly violates Section 553 of the APA. Even if this Court were to agree with the Federal Circuit's reading of the relevant statutes in this case, and it should not read the statutes in that manner based on the plain language of 35 U.S.C. § 154(c)(1), this Court should grant a writ of *certiorari*, reverse the decision of the Federal Circuit in part, and remand this case to the Federal Circuit with instructions to further remand this case to the District Court and then to the FDA, so that the FDA may comply with the APA. Otherwise, permitting the FDA's action to stand will establish precedent for federal agencies to ignore with impunity the mandates of the APA and permit them to adopt new rules which affect the industries they regulate without the requisite notice-and-comment rulemakings.

CONCLUSION

For all of the reasons set forth in this Petition, Petitioner Organon Inc. respectfully submits that this Court should issue a writ of *certiorari* to the United States Court of Appeals for the Federal Circuit in this matter.

Respectfully submitted,

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APPENDIX A

United States Court of Appeals
for the Federal Circuit

96-1068, -1105, -1107

MERCK & CO., INC. AND MSD TECHNOLOGY, L. P.,

Plaintiffs-Appellees,

and

SCHERING CORPORATION,

Plaintiff-Appellee,

and

BRACCO DIAGNOSTICS INC. AND
BRACCO INTERNATIONAL B.V.,

Plaintiffs-Appellees,

and

HOFFMANN-LA ROCHE INC. and
SYNTEX (U.S.A.) INC.,

Plaintiffs-Appellees,

and

ORGANON, INC.,

Plaintiff-Appellee,

v.

DAVID A. KESSLER, M.D.,
Commissioner of Food and Drugs, and
BRUCE A. LEHMAN, Assistant Secretary
of Commerce and
Commissioner of Patents and Trademarks,

Defendants-Appellants,

and

GENERIC PHARMACEUTICAL
INDUSTRY ASSOCIATION,

Defendant-Appellant.

DECIDED: April 4, 1996

Before ARCHER, *Chief Judge,* NIES, *Senior Circuit Judge,* MICHEL, *Circuit Judge,* NIES, *Senior Circuit Judge.*

These appeals raise the question of whether there are limitations to the application of a patent restoration extension, granted pursuant to the Hatch-Waxman Act (35 U.S.C. § 156), to the term of the patent calculated as 20 years from filing under the Uruguay Round Agreements Act (URAA) (35 U.S.C. § 154). The district court held that all patents in force on June 8, 1995, including patents in force only because of a Hatch-Waxman extension, were entitled to add the time of the Hatch-Waxman extension to the new term afforded by the URAA. We affirm-in-part and reverse-in-part.

I.

Two statutes are at issue in this case. The Drug, Price Competition and Patent Term Restoration Act, codified in part at 35 U.S.C. § 156,[1/] (also known as the Hatch-Waxman Act), provides generally for a limited extension of the term of a patent, *inter alia,* for a drug as to which marketing was held up during the patent term by the process of obtaining Food and Drug Administration (FDA) approval (hereinafter "restoration extension"). Each of the drug patents in suit received a two-year restoration extension at a time when the term of the patent was 17 years from date of issuance. The second statute is the URAA, 35 U.S.C. § 154 (1995), which provides an alternative calculation of the term for patents in force on

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[1/] Unless otherwise noted, all citations to the U.S. Code are to the 1988 edition.

June 8, 1995, namely, 20 years from filing of the patent application. For patents that were prosecuted to issuance in less than three years, URAA effects an extension of its term, that is, the difference between 17 years from issuance and 20 years from filing. Each of the patents in suit was in force on June 8, 1995.

The first of these statutes, the Hatch-Waxman Act, which passed in 1984, eliminated the pre-1984 requirement that a company seeking to market a generic version of a patented drug had to conduct its own testing program. Instead, the Hatch-Waxman Act permits the generic producer of the fully tested drug to rely on the safety and efficacy data of a prior applicant, frequently the holder of a patent on the product. 21 U.S.C. § 355(j)(7)(B); H.R. Rep. No. 857, 98th Cong. 2d Sess. Pt. 1, at 16-17 (1984). Thus, the marketing of generic versions of an FDA-approved drug is expedited. In exchange, the Hatch-Waxman Act provides the holders of patents on approved patented products with an extended term of protection under the patent to compensate for the delay in obtaining FDA approval. This restoration period does not recover the full time lost from the patent term due to FDA's premarket approval process but merely "ameliorates the loss incurred when patent terms tick away while the patented product is awaiting [FDA's] regulatory approval for marketing." *Unimed, Inc. v. Quigg*, 888 F.2d 826, 829, 12 USPQ2d 1644, 1647 (Fed. Cir. 1989). Regardless of the time so lost, if a patent was issued and testing began before the 1984 enactment of the Hatch-Waxman Act, the total extension period may not exceed two years, 35 U.S.C. §

156(g)(6)(C); otherwise the restoration period is limited to no more than five years. *Id.* at § 156(g)(6)(B). Further, the effective patent term including the restoration period may not exceed 14 years following FDA approval of the new drug. *Id.* at § 156(c)(3).

Another overall limitation is that the term of the patent may be given only one restoration extension. *Id.* at § 156(a)(2). If the term of the patent has received such an extension, the patent may not be given another restoration extension even for another drug covered by the patent whose marketing also is delayed by reasons of FDA procedures. Finally, the restoration period of the patent does not extend to all products protected by the patent but only to the product on which the extension was based. *Id.* at § 156(b)(1). A restoration extension is made known to the public by the issuance of a certificate by the PTO stating the number of days that the term is extended. *Id.* at § 156(e)(1); 37 C.F.R. § 1.780.

The FDA has major administrative responsibilities under the Hatch-Waxman Act. A generic drug manufacturer is not guilty of infringement by filing an application for approval of marketing (an ANDA) if the generic company does not seek approval to engage in the commercial manufacture, use, or sale of the drug before the expiration of the patent. On the other hand, a patent owner is entitled to notice, and it is an act of infringement for purposes of a declaratory judgment action, for a generic manufacturer to file an ANDA for use prior to the patent

expiration date on the basis of alleged invalidity or noninfringement of the patent. The statute requires the FDA to publish the expiration date, and a patent owner must be given notice by the applicant of an ANDA seeking use before the expiration of the patent.[2/]

The second statute, the URAA, was enacted in 1994. The purpose of the URAA was not to extend patent terms, although it has that effect in some cases, but to harmonize the term provision of United States patent law with that of our leading trading partners which grant a patent term of 20 years from the date of filing of the patent application. Prior to June 8, 1995, U.S. patents had an expiration date under 35 U.S.C. § 154 measured as 17 years from the date the patent issued, except where terminal disclaimers were filed. Amended section 154(a) now reads:

> Subject to the payment of fees under this title, such grant shall be for a term beginning on the date on which the patent issues and ending 20 years from the date on which the application for the patent was filed in the United States or, if the

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[2/] A detailed explanation of the workings of the Hatch-Waxman Act is provided by the recent opinion of this court in *Bristol-Myers Squibb Co. v. Royce Laboratories, Inc.*, 69 F.3d 1130, 36 USPQ2d 1641 (Fed. Cir. 1995), *cert. denied*, 116 S. Ct. 754 (1996).

> application contains a specific reference to an earlier filed application or applications under section 120, 121, or 365(c) of this title, from the date on which the earliest such application was filed.

35 U.S.C. § 154(a)(2) (1994).

For certain patents which were issued and for pending applications which were filed prior to June 8, 1995, a transitional provision preserves a guaranteed 17-year term, if it is longer than 20 years from filing, by the following provision:

> The term of a patent that is in force on or that results from an application filed before the date that is 6 months after the date of the enactment of the Uruguay Round Agreements Act shall be the greater of the 20-year term as provided in subsection (1), or 17 years from grant, subject to any terminal disclaimers.

Id. at § 154(c)(1). Patents in the section 154(c)(1) category thus are entitled to keep or to enjoy the 17-year term from issuance of the patent or a 20-year from filing term, whichever is longer.[3/]

[3/] The provisions for extension in section 154 are (continued...)

Congress did not expressly address the question whether a restoration extension under section 156 could be added to the term of a patent which could also invoke the section 154 transition provision. Delineating the combined effects of the URAA and the Hatch-Waxman Act for patents issued prior to June 8, 1995, is thus the task before us.[4/] It is agreed that a patent issued after June 8, 1995, on a transition application is entitled to any applicable restoration extension to be added to its term which is 17 years from issuance or 20 years from filing whichever is longer.

[3/](...continued)
more complicated than the above-quoted provision alone and include extensions for delay attributable to appellate review. The revised section 154 also includes a limitation on remedies under 35 U.S.C. §§ 283, 284, and 285 against infringers who made a substantial investment before the expiration of the original 17-year term. However, remedies under section 271(e)(4) remain the same. *See Bristol-Myers,* 69 F.3d 1130.

[4/] The court acknowledges with appreciation the briefs *amici curiae* filed by Public Citizen, National Council of Senior Citizens, National Consumers League, National Association of Pharmaceutical Manufacturers, National Pharmaceutical Alliance, Gray Panthers, United States Health Cooperative, Hovione Sociedade Quimica, S.A., and the Pharmaceutical Research and Manufacturers of America.

II.

The plaintiffs in these actions are holders of patents in force on June 8, 1995. When each of the 12 patents in this case was issued, it received a term of 17 years from its grant, pursuant to the then-existing provisions of section 154. Also prior to the URAA's effective date of June 8, 1995, each of these patents received a two-year restoration extension pursuant to the Hatch-Waxman Act. Five of the patents in issue were "in force" only because the patent term had been given a restoration extension.

On enactment of 35 U.S.C. § 154, these plaintiffs submitted to the FDA requests for publication of new patent expiration dates. As explained above, the FDA is required to publish patent expiration dates in connection with administering the Hatch-Waxman Act. Each of the plaintiff patent holders submitted new expiration dates for their patents based on a term calculated as 20 years from the filing date of the patent application plus two years. The FDA refused to publish the new expiration dates calculated by these patent holders. The basis for the refusal was the issuance by the Commissioner of Patents and Trademarks (the "PTO") of a "Final Determination" which, in effect, ruled that the holder of a patent which was granted before June 8, 1995, was not entitled to have a restoration extension, previously received or one obtained

in the future, added to the end of the 20-year term provided under amended section 154.[5/]

With respect to patents issued before June 8, 1995, the PTO and FDA took the position that the patentee is entitled to 17 years from issuance plus any restoration extension or to 20 years from filing (without a restoration add-on), whichever is greater. For each of the patents in suit, the 20-year from filing term is shorter than the existing term under the PTO interpretation so that the patentee has no claim to a 20-year from filing term. The PTO principally relied on the language in section 156(a) that the term of a patent "shall be extended in accordance with this section from the original expiration date of the patent . . ." (emphasis added). Inasmuch as any patent issued prior to June 8, 1995, was granted a term of 17 years from issuance, the PTO concludes that that date is its "original expiration date" and the restoration extension can only be added thereto. The PTO also notes that, for at least one patent in issue, adding the restoration extension to the 20-year term violates the 14-year cap of section 156(c)(3), absent recalculation. Nothing added to the patent statute by URAA mandates such a recalculation of a restoration extension.

The district court rejected the PTO/FDA interpretation. The district court found that that interpretation would have a disparate impact on those

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[5/] 60 Fed. Reg. 30,069-71 (1995).

patent applicants whose filing preceded June 8, 1995, and those applicants who filed thereafter. In the court's view, it would be inconsistent with the apparent even-handedness intended by the URAA to discriminate between these two groups on the basis of filing date of the application. The court rejected the PTO's reliance on the words "original expiration date" in section 156(a), reasoning that the URAA, in effect, changed the "original expiration date" in some cases to mean 20 years from the filing date of the application. As to patents which would have expired prior to June 8, 1995, but for a restoration extension, the court was unpersuaded that permitting a two-year restoration extension to be added anew to a URAA extended term was prohibited under the Hatch-Waxman Act as a "second" extension. The court adhered to this conclusion even where the effective restoration period exceeded the two-year and fourteen-year time limitations for Hatch-Waxman extensions.

III.

A. Jurisdiction

As an initial matter, this court questioned the propriety of reviewing at this time the PTO's "Final Determination" in a declaratory judgment action. Was the question of its correctness raised in a case or controversy? U.S. Const. art. III, § 2. Upon review of all of the circumstances, we hold that the constitutional limitation on review is satisfied. The dispute arose between appellees and the FDA, which refused to publish new expiration

dates pursuant to a claim of entitlement under URAA. In that connection, the PTO's ruling may be reviewed inasmuch as the FDA adopted the PTO's interpretation of the statute as the basis for its action. Further, appellants are damaged by reason of their entitlement to notice from generic manufacturers depending on the patent expiration date which they would not receive without publication of the new date. An actual case or controversy is presented. Cf. *DuPont Merck Pharmaceutical Co. v. Bristol-Myers Squibb Co.*, 62 F.3d 1397, 35 USPQ2d 1718 (Fed. Cir. 1995).

B. *Standard of Review*

Respecting our review of the merits, we are presented with a matter of pure statutory interpretation. Accordingly, this court reviews the district court's decision on the meaning of the various provisions and their interrelationship *de novo*. *Bristol-Myers Squibb Co. v. Royce Labs., Inc.*, 69 F.3d 1130, 1134, 36 USPQ2d 1641 1645 (Fed. Cir. 1995), *cert. denied*, 116 S. Ct. 754 (1996).

Commissioners Kessler and Lehman contend that "under the familiar instructions of the Supreme Court in *Chevron*, 467 U.S. at 844, PTO's Final Determination is entitled to controlling weight." The contention is unavailing, based as it is on a mistake as to *Chevron's* breadth. Under *Chevron*, where Congress has authorized an agency to promulgate substantive rules under a statute it is charged with administering, we must uphold the

agency's interpretation of an ambiguity or omission in that statute if the interpretation is a reasonable one. *Chevron, U.S.A., Inc. v. Natural Resources Defense Council, Inc.*, 467 U.S. 837, 842-45 (1984). As the Seventh Circuit recently had occasion to note, however, "only statutory interpretations by agencies with rulemaking powers deserve substantial deference." *Atchison, Topeka and Santa Fe Ry. Co. v. Pena*, 44 F.3d 437, 441 (7th Cir. 1994) *(in banc)* (emphasis added), *aff'd*, 116 S. Ct. 595 (1996). *See also* 1 KENNETH CULP DAVIS AND RICHARD J. PIERCE, JR., ADMINISTRATIVE LAW TREATISE § 6.3 (1994); Michael Herz, *Deference Running Riot: Separating Interpretation and Lawmaking Under Chevron*, 6 Admin. L.J. Am. U. 187, 200-03 (1992).

As we have previously held, the broadest of the PTO's rulemaking powers--35 U.S.C. § 6(a)--authorizes the Commissioner to promulgate regulations directed only to "the conduct of proceedings in the [PTO]"; it does not grant the Commissioner the authority to issue substantive rules. *Animal Legal Defense Fund v. Quigg*, 932 F.2d 920, 930, 18 USPQ2d 1677, 1686 (Fed. Cir. 1991).[6/] Because Congress has not vested the Commissioner with any

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[6/] Accord *Hoechst Aktiengesellschaft v. Quigg*, 917 F.2d 522, 526, 16 USPQ2d 1549, 1552 (Fed. Cir. 1990); *Glaxo Operations UK Ltd. v. Quigg*, 894 F.2d 392, 398-99, 13 USPQ2d 1628, 1632-33 (Fed. Cir. 1990); *Ethicon Inc. v. Quigg*, 849 F.2d 1422, 1425, 7 USPQ2d 1152, 1154 (Fed. Cir. 1988).

general substantive rulemaking power, the "Final Determination" at issue in this case cannot possibly have the "force and effect of law." *Chrysler Corp. v. Brown,* 441 U.S. 281, 302 (1979) ("[T]he exercise of quasi-legislative authority by governmental departments and agencies must be rooted in a grant of such power by the Congress and subject to limitations which that body imposes."). Thus, the rule of controlling deference set forth in *Chevron* does not apply. Such deference as we owe to the PTO's interpretive "Final Determination" regarding the interrelationship by the URAA and the Hatch-Waxman Act thus arises, not from the rule of *Chevron,* but solely from, *inter alia,* the thoroughness of its consideration and the validity of its reasoning, *i.e.,* its basic power to persuade if lacking power to control. *See E.E.O.C. v. Arabian American Oil Co.,* 499 U.S. 244, 257 (1991); *General Elec. Co. v. Gilbert,* 429 U.S. 125, 140-46 (1976); *Skidmore v. Swift & Co.,* 323 U.S. 134, 140 (1944).

IV.
MERITS

The PTO/FDA argues that, as a matter of statutory interpretation, no patent issued before June 8, 1995, is entitled to add on any restoration extension to the 20-year from filing term whether the extension was granted before that date or is obtained in the future. With respect to the five patents which were in force only because the restoration period had been added to the 17-year term, the

PTO/FDA goes further and argues that reapplication of a restoration period in these instances, as directed by the district court, would violate specific provisions of the statute. Appellant GPIA takes the position that the allowance of an extension for a pre-June 8, 1995, patent depends on when the extension was granted. Thus, patents issued before June 8, 1995, but which received extensions after that date, would add on that time, but restoration extensions given before June 8, 1995, would attach only to the 17-year from issuance term. The district court rejected both of these views, ruling that all patents in force on June 8, 1995, are entitled to add a restoration extension to a term calculated as 20 years from filing, regardless of when the extension is granted.

For reasons which follow, we conclude that pre-June 8, 1995, patents are entitled to add on the restoration extension to a 20-year from filing term regardless of when such extension is granted except for those patents kept in force on June 8, 1995, only because of a restoration extension. Under this interpretation, all provisions of both URAA and Hatch-Waxman can reasonably be given effect. Thus, we affirm-in-part and reverse-in-part.

We disagree with the PTO that the statutory language of section 156(a)(2), *i.e.*, "original expiration date," can mean only the date of expiration when the patent was granted. The legislative history indicates that the phrase "original expiration date" was inserted in

association with the limitation that to receive a restoration extension "the term of the patent ha[d] never been extended" by a prior restoration extension.[7/] Indeed, the only amendment made to Hatch-Waxman by the URAA was to make this explicit. Section 156 now reads that a restoration extension may not be given if the patent has been "extended under subsection(e)(1) of this section." 35 U.S.C. § 156(a)(2) (1994) (emphasis added). Clearly, a patent may receive only one restoration extension. However, we do not agree with the PTO/FDA that this section presents a linguistic barrier to an add-on to a term

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[7/] In June of 1982, Congressman Tom Railsback sent a letter to Mr. Bruce Lehman, then Counsel to the Subcommittee on Courts, Civil Liberties, and the Administration of Justice, detailing technical amendments to H.R. 6444, a 1982 predecessor of the Hatch-Waxman Act. One of the amendments added the language "from the original expiration date of the patent." Regarding this change, Congressman Railsback stated:

> The insertion of "from the original expiration date of the patent" on line 6, makes specific what was intended, namely, that the maximum extension of 7 years [enacted as 5 years], must be calculated from the original expiration date of the patent. Thus, 2 five-year regulatory review periods for 2 different products under the same patent will result in only one extension from the original patent expiration date.

extended by URAA. We conclude that "original expiration date" means no more than that the expiration date has not been extended under section 156(e)(1) and, thus, the phrase can identify more than one date.

As evidence of this meaning, it must be noted that 35 U.S.C. § 154(b)(2) provides for a term extension where issuance of a patent is delayed due to appellate review of an adverse determination of patentability. This new type of extension could be determined and granted post-issuance and would be added to the term prior to the addition of a restoration extension which, under section 156(a), is added to the end of what otherwise would be the patent term. Thus, the "original expiration date" of such patent would be its expiration date with the appellate review extension added, *i.e.*, such patent's "original expiration date" would not be the expiration date at the grant of the patent. Nothing in the amendment effecting appellate review extensions suggests otherwise. Thus, we do not find the argument persuasive that, in all instances, the "original expiration date" for a pre-URAA patent must be fixed at 17 years from issuance under section 156(a). The statute, as amended, requires a more flexible interpretation of the phrase "original expiration date." Accordingly, we see no impediment to applying the restoration extension to a 20-year from filing term by reason of this statutory language.

In some instances, there may be a problem in adding a restoration extension granted pre-URAA to the 20-year term. Under the Hatch-Waxman Act the patent

term plus any restoration extension cannot exceed 14 years from the date of FDA approval. 35 U.S.C. § 156(c)(3). With respect to any restoration period granted after June 8, 1995, this 14-year limitation would be part of the calculation of the permissible number of days of the restoration extension. However, the addition of a pre-URAA restoration extension to a post-URAA term might extend past the 14-year limit. Congress has clearly spoken to this point. The 14-year period is a mandatory limit on the extended term and must be given effect. Thus, some pre-June 8, 1995, extensions may need adjustment. GPIA argues for denial of pre-URAA restoration extensions precisely because FDA would have to recalculate the allowable number of days to insure that the 14-year restriction is met. We do not agree with appellants that pre-URAA patentees should be denied restoration extensions for this reason. GPIA's interpretation would treat otherwise equal patents unequally depending upon when the patentee applies for and the FDA grants an extension. Correction to fit within the 14-year limitation entails only a purely ministerial task, no more taxing than the recalculation of a new date for a patent extended by URAA alone (that is, without a restoration extension).[8/]

[8/] The district court did not address the 14-year limitation problem. However, the new expiration date calculated for U.S. Patent No. 4,283,408 exceeds this limit. On remand, the term of this patent must be calculated to

(continued...)

More troubling is the problem of fitting together the different limitations on remedies during successive extensions. For pre-June 8, 1995, patents, a patentee would have full exclusionary rights for 17 years, followed by rights only to equitable remuneration (neither lost profits, an injunction, punitive damages, nor attorney fees) with respect to a certain class of infringers for the period from the end of the 17-year term to the end of the new 20-year term (the delta period), followed by entitlement to full exclusionary rights but only with respect to the approved product during the period of the restoration extension.

Upon analysis, however, this problem is more illusory than real. Infringers of drug patents who qualify for the relief afforded during the delta period are few and will diminish. The delta period limitation applies only to patents granted before June 8, 1995.[9] Further, the infringing acts, or preparation for such acts, must have

---

[8](...continued)
expire no later than 14 years after FDA marketing approval.

[9] All patents issued after June 8, 1995, are granted with the longer of the two possible terms. No competitor could commit any acts in reliance on an earlier expiration date. Thus, there is no delta period for such patents even though based on an application filed before June 8, 1995.

begun prior to June 8, 1995, a date which will be increasingly hard to meet. In addition, unlike other manufacturers who may benefit from the delta period, a generic drug manufacturer must obtain FDA approval for marketing its product, now usually by an ANDA. Such a manufacturer is not entitled to go forward with marketing an infringing drug during the delta period without subjecting itself to suit for infringement. *DuPont Merck*, 62 F.3d 1397, 35 USPQ2d 1718. FDA will not approve a generic for marketing under an ANDA where the patentee files suit until the patent has expired, 30 months have passed since the patentee received notice of the ANDA, or the suit is resolved. The length of the delta period can be expected to expire before 30 months. Indeed, in view of the limited time of a delta extension--in all cases substantially less than three years--the problem will be nonexistent in most cases.

If some situations arise where full patent rights are restored for the approved product after an infringer markets a generic drug during a delta period, these can be handled on a case-by-case basis. We conclude that the majority of patents should not be denied extensions because of a mere possibility that special problems may arise in a few instances. The statute contemplates a patentee receiving time lost in its patent term by reason of FDA delay, and the statute should be liberally interpreted to achieve this end.

This leaves for consideration the five patents at issue in this proceeding which were in force on June 8,

1995, only by virtue of having previously received a restoration extension which became operative before that date. With respect to these patents, we must agree with the PTO/FDA position that application of the restoration extension violates specific provisions of the Hatch-Waxman Act and, unlike the 14-year limitation, a minor adjustment does not bring them into conformity. Section 156(a)(2) provides that a restoration extension may be given provided "the term of the patent has never been extended under subsection (e)(1) of this section." The terms of these five patents have once been extended under subsection (e)(1). Indeed, it is only because of actual use of the restoration extension that the patentees can even make their arguments under the Hatch-Waxman Act. A reapplication of the restoration extension would constitute a second extension contrary to the statute.

In addition, Congress has specifically limited any restoration extension for these patents to two years. By first applying the extension to its original 17-year term, and now applying the full extension again to the new term, this limit would be exceeded. For example, U.S. Patent No. 4,001,323 would have expired on January 4, 1994, before enactment of the URAA. It received the maximum extension of two years and had used 17 months of that extension as of June 8, 1995. Under the district court's interpretation, the patentee is entitled to the two-year extension added to a 20-year term. The restoration extension totals 41 months, which exceeds the statutory limit of 24 months. Congress would have had to amend section 156(g)(6)(c) to lift this limitation for partially used

extensions, either to exceed the two-year limit or to allow the time of a restoration extension to be split. No one argues that the statute allows splitting extensions. In any event, Congress made neither change, although, as indicated, it did amend one section of the Hatch-Waxman Act as part of the URAA. Thus, we presume it did not intend to lift this ban. This court would simply have to rewrite the statute.

The district court ruled for the patentees on this point because it believed Congress intended that applications filed before URAA should be treated the same as patent applications filed after. However, Congress itself treated these two classes of applications differently. No patent issued on an application filed after June 8, 1995, has a guaranteed 17-year term. With the two-year limitation, Congress struck the balance it wished between restoration extensions and early availability of generics. The two-year limitation, accordingly, cannot be judicially skirted.

Finally, the problem of different remedies is not illusory for these previously extended patents. The restriction of enforcement to one product had already occurred before URAA took effect. To follow this period of limited enforcement with enforcement for all products covered by the patent (or delta enforcement in some cases) and then return to one product enforcement again can only be characterized as bizarre. No principle of statutory construction allows us to ignore specific statutory provisions or adopt an unreasonable construction.

In sum, patents that were in force on June 8, 1995, only because of a Hatch-Waxman extension are not entitled to reapply a restoration extension to a 20-year from filing term. Except for those patents, a patent in force on June 8, 1995, is entitled to have a restoration extension, whenever granted, added to the longer term of either 17 years from issuance or 20 years from filing.

V.
CONCLUSION

For the foregoing reasons we affirm in part, reverse in part, and remand to the district court for amendment of its order in accordance with this opinion.

VI.
COSTS

Each party will bear its own costs.

AFFIRMED-IN-PART, REVERSED-IN-PART AND REMANDED

APPENDIX B

IN THE UNITED STATES DISTRICT COURT FOR THE
EASTERN DISTRICT OF VIRGINIA
ALEXANDRIA DIVISION

ORGANON, INC.,	)	
Plaintiff,	)	
	)	
v.	)	CIVIL ACTION
	)	NO. 95-1380-A
DAVID A. KESSLER, M.D.,	)	
COMMISSIONER	)	
OF FOOD AND DRUGS,	)	
et al.,	)	
	)	
Defendants.	)	

MEMORANDUM OPINION

This case presents the same issues raised in the patent cases decided by this court's October 16, 1995, Memorandum Opinion and Order in Civil Action Nos. 95-1005-A, 95-1052-A, 95-1103-A, and 95-1236-A. The court concludes for the same reasons set forth in that Memorandum Opinion and Order that summary judgment should be awarded to the plaintiff. On that basis, the same injunctive and declaratory relief accorded to the plaintiffs in that action is awarded to this plaintiff. The expiration date of this plaintiff's patent is therefore declared to be November 6, 1996.

The Memorandum Opinion and Order of October 16, 1995, are attached and made a part of this Memorandum Opinion. The court deems it inappropriate to invoke alternative constitutional bases for its decision, and declines the plaintiff's invitation to address the constitutional issues where the matter can be resolved by statutory interpretation.

/s/ Albert V. Bryan, Jr.
United States District Judge

Alexandria, Virginia
November 9, 1995

IN THE UNITED STATES DISTRICT COURT FOR THE
EASTERN DISTRICT OF VIRGINIA
ALEXANDRIA DIVISION

ORGANON, INC.,	)	
Plaintiff,	)	
	)	
v.	)	CIVIL ACTION
	)	NO. 95-1380-A
DAVID A. KESSLER, M.D.,	)	
COMMISSIONER	)	
OF FOOD AND DRUGS,	)	
et al.,	)	
	)	
Defendants.	)	

ORDER

For the reasons set forth in the Memorandum Opinion and order of October 16, 1995, in Civil Action Nos. 95-1005-A, 95-1052-A, 95-1103-A, and 95-1236-A, and in the Memorandum Opinion this day filed, it is hereby

ORDERED that plaintiff's motion for summary judgment is granted, and the plaintiff's proper patent expiration date is November 6, 1996.

/s/ Albert V. Bryan, Jr.
United States District Judge

Alexandria, Virginia
November 9, 1995

APPENDIX C

IN THE UNITED STATES DISTRICT COURT FOR THE
EASTERN DISTRICT OF VIRGINIA
ALEXANDRIA DIVISION

MERCK & CO., INC., et al.,	)	
	)	
Plaintiffs,	)	
	)	
V.	)	CIVIL ACTION
	)	No. 95-1005-A
DAVID A. KESSLER, M.D., Commissioner of Food and Drugs, et al.,	)	
	)	
Defendants.	)	
	)	
SCHERING CORPORATION,	)	
	)	
Plaintiff,	)	
	)	
V.	)	CIVIL ACTION
	)	No. 95-1052-A
DAVID A. KESSLER, M.D., Commissioner of Food and Drugs, et al.,	)	
	)	
Defendants.	)	
	)	

BRACCO DIAGNOSTICS INC., et al.,	)	
Plaintiffs,	)	
V.	)	CIVIL ACTION
	)	No. 95-1103-A
BRUCE A. LEHMAN, Assistant Secretary of Commerce and Commissioner of Patents and Trademarks,	)	
Defendant.	)	
HOFFMANN-La ROCHE INC., et al.	)	
Plaintiffs,	)	
V.	)	CIVIL ACTION
	)	No. 95-1236-A
BRUCE A. LEHMAN, Assistant Secretary of Commerce and Commissioner of Patents and Trademarks,	)	
Defendant.	)	

MEMORANDUM OPINION

Effective June 8, 1995, as a result of the enactment of the Uruguay Round Agreements Act (URAA), the terms

of patents formerly seventeen years from the date the patent issued, was changed as follows:

> Subject to the payment of fees under this title, such grant shall be for a term beginning on the date on which the patent issues and ending 20 years from the date on which the application for the patent was filed in the United States or, if the application contains a specific reference to an earlier filed application or applications under section 120, 121, or 365(c) of this title, from the date on which the earliest such application was filed.

35 U.S.C. § 154(a)(2).

A transitional provision provided as follows:

> The term of a patent that is in force on or that results from an application filed before the date that is 6 months after the date of the enactment of the Uruguay Round Agreements Act shall be the greater of the 20-year term as provided in subsection (1), or 17 years from grant, subject to any terminal disclaimers.

35 U.S.C. § 154(c)(1).

The issue in these cases is whether extension or restoration rights of patent terms which have been allowed pursuant to 35 U.S.C. § 156 (The Waxman-Hatch Act) for a time equal to the regulatory review period (two years insofar as these cases are concerned) can be used to extend the twenty year period as to patents which are in force on June 8, 1995.[1/] In other words, can a holder of a patent in force on June 8, 1995, add a previously granted patent restoration period to a twenty year term in determining when the patent expires.

On June 7, 1995, the Patent and Trademark Office (PTO) published a "Final Determination" which in effect ruled that the holder of such a patent must choose between a term of seventeen years from grant of the patent plus a restoration period, or a term of twenty years from filing without the restoration period.

The Food and Drug Administration (FDA), charged with publication of patent expiration dates submitted by holders of patents in force on June 8, 1995, has refused to publish expiration dates calculated in a manner inconsistent with the ruling of the PTO.

[1/] Some of the patents at issue in these cases had not expired as of June 8, 1995, because the seventeen years had not run, and some of the patents at issue were in force as of June 8, 1995, only because they had previously been granted regulatory review extensions.

The plaintiffs in these actions are holders of patents in force on June 8, 1995, which have previously been accorded restoration rights and who have been refused publication of their submitted expiration dates by the FDA because of the PTO ruling. The plaintiffs challenge the actions of the FDA and the PTO and seek declaratory judgments that the actions are unlawful, that their patents expire only after twenty years, plus the previously granted restoration right, and injunctive relief in the form of a direction to the FDA to publish and a withdrawal by the PTO of the Final Determination ruling.

The actions are before the court on the plaintiffs' motions for summary judgment. The government has responded with a motion to dismiss, which is in reality a cross motion for summary judgment. Permitted to intervene and participate in the argument in support of the government's position was the Generic Pharmaceutical Industry Association (GPIA). This is a national trade association whose members include the majority of the manufacturers of generic pharmaceutical, who obviously have an interest in when patents on pharmaceuticals, the types of patents at issue in this case, expire.

* * *

It is conceded that any patent applied for after June 8, 1995, would be for twenty years and would have the benefit of any extension available to it under 35 U.S.C. § 156. The URAA is silent as to the application of regulatory review extensions to the twenty year term. It seems apparent to the court, however, that the URAA's change of the term length was to do no more than bring United States patent law into closer harmony with the laws

of other developed nations. Its transitional provision, by providing that the patent term is to apply to previously issued patents, is further indication that no differentiation in restoration rights for patents with the later life was intended. Many statutory enactments draw lines, and some form of prejudice or benefit can accrue depending on which side of the line a party ends up on after the enactment. But the disparate impact on those patent applicants who precede June 8, 1995, and those who follow, which would result from [t]he PTO's Final Determination, is inconsistent with the apparent even-handedness intended by the URAA. To draw the inference that the URAA was intended to or did operate to strip from patents in force on June 8, 1995, the carefully drafted regulatory review extensions merely because that act lengthened the patent term from seventeen to twenty years, is not warranted.

The government places its primary argument on the use of the term "original expiration date" as used in The Hatch-Waxman Act. 35 U.S.C. § 156(a), in providing for extensions, is worded as follows:

> The term of a patent which claims a product, a method of using a product, or a method of manufacturing a product shall be extended in accordance with this section from the <u>original expiration date</u> of the patent if.... (Emphasis supplied.)

The government argues that this can only mean the original expiration date from a patent whose term is

seventeen years. This is too narrow a construction. The URAA in effect extended the original expiration date to twenty years from the date of application. It effected a change in the "term" as used in § 156(a) and § 156(c).

Nor is the court persuaded by the asserted complicated recalculation involved in the sixty day provision and fourteen year limitation set forth in 35 U.S.C. § 156(d)(1) and § 156(c)(3), respectively.

The court is likewise unpersuaded by the argument, principally made by the intervenor, that permitting the two year regulatory review extension to be added to the twenty year term for the patents at issue in this case is somehow a second extension which is prohibited by Waxman-Hatch. The only extension which results from adding the two years to the twenty years is the extension applied to the terms of all patents by the URAA. This was no more a windfall to the plaintiffs than the windfall which benefitted many patent holders when the seventeen year term of patents was extended to twenty years.

A substantial portion of the defendants' brief is directed to the deference owed an agency's determination. In the court's view, this is not an issue in the case. Resolution of what the court perceives to be the issues involved here, is a straightforward matter of statutory interpretation.

The declaratory and injunctive relief requested by the plaintiffs will be granted,[2/] and the court will declare the eleven patents in issue to have the expiration dates dictated by allowing the previously granted extension to be added to the twenty year term.

/s/ Albert V. Bryan, Jr.
United States District Judge

Alexandria, Virginia
October 16, 1995

2/ The patents at issue in this action all have had extensions previously granted. Because the rationale of the court's ruling applies to extensions available in the future, the declaratory and injunctive relief applies to patents in force on June 8, 1995, but which may be entitled to extensions in the future.

IN THE UNITED STATES DISTRICT COURT FOR THE
EASTERN DISTRICT OF VIRGINIA
ALEXANDRIA DIVISION

MERCK & CO., INC., et al.,	)	
	)	
Plaintiffs,	)	
	)	
V.	)	CIVIL ACTION
	)	No. 95-1005-A
DAVID A. KESSLER, M.D., Commissioner of Food and Drugs, et al.,	)	
	)	
Defendants.	)	
	)	
SCHERING CORPORATION,	)	
	)	
Plaintiff,	)	
	)	
V.	)	CIVIL ACTION
	)	No. 95-1052-A
DAVID A. KESSLER, M.D., Commissioner of Food and Drugs, et al.,	)	
	)	
Defendants.	)	
	)	
BRACCO DIAGNOSTICS INC., et al.,	)	
	)	
Plaintiffs,	)	

	)
V.	) CIVIL ACTION
	) No. 95-1103-A
BRUCE A. LEHMAN, Assistant	)
Secretary of Commerce and	)
Commissioner of Patents	)
and Trademarks,	)
Defendant.	)
	)
HOFFMANN-La ROCHE INC.,	)
et al.	)
	)
Plaintiffs,	)
	)
V.	) CIVIL ACTION
	) No. 95-1236-A
BRUCE A. LEHMAN, Assistant	)
Secretary of Commerce and	)
Commissioner of Patents	)
and Trademarks,	)
Defendant.	)

ORDER

Upon consideration of the arguments and submissions of the parties and for the reasons set forth in the Memorandum Opinion this day filed, it is hereby ADJUDGED, ORDERED and DECLARED that:

1. These actions are consolidated.

2. The motion of Generic Pharmaceutical Industry Association (GPIA) to intervene is granted.

3. The motion of the plaintiffs for summary judgment are granted.

4. The motion of David A. Kessler, M.D., Commissioner of Food and Drug (FDA), and Bruce A. Lehman, Commissioner of Patents and Trademarks (PTO), and the intervenor to dismiss and for summary judgment are denied.

5. The Final Determination of the PTO published in the Federal Register at 60 Fed. Reg. 30069 on June 7, 1995, is invalid and unenforceable.

6. The expiration dates for the patents at issue in this action are as follows:

Patent No.	Holder	Exp. Date (w/20 +2)
4,001,323	Bracco	11/24/97
4,282,233	Schering	6/19/02
4,283,408	Merck	10/15/00
4,146,719	Merck	2/16/00
4,231,938	Merck	6/15/00
4,316,839	Roche	10/10/04
4,278,663	Roche	1/30/03
4,078,071	Syntex	7/28/97
4,089,969	Syntex	7/14/89
4,355,032	Syntex	6/23/03
3,985,758	Syntex	2/15/96

7. For patents entitled to a term of the greater of twenty years from patent filing or seventeen years from grant, under 35 U.S.C. § 154(c)(1), periods of restoration of patent life that have been granted, or that will be granted under 35 U.S.C. § 156, are added to that term.

8. The refusal of the FDA to publish the above expiration dates as submitted by the plaintiffs is invalid and unlawful.

9. The FDA shall withdraw its Notice declining to publish the above expiration dates in the "Orange Book" as proper expiration dates submitted by the plaintiff, and shall publish those dates in the Orange Book.

10. The Final Determination of the PTO, mentioned above, shall be withdrawn by the PTO.

11. The FDA is prohibited from approving any abbreviated new drug applications, abbreviated new animal drug application or applications filed under 21 U.S.C. § 355(b)(2) that do not take into account the expiration dates of patents as determined by this order.

/s/ Albert V. Bryan, Jr.
United States District Judge

Alexandria, Virginia
October 16, 1995

APPENDIX D

IN THE UNITED STATES DISTRICT COURT FOR THE
EASTERN DISTRICT OF VIRGINIA
ALEXANDRIA DIVISION

ORGANON, INC.,	)	
	)	
Plaintiff,	)	
	)	
v.	)	CIVIL ACTION
	)	NO. 95-1380-A
DAVID A. KESSLER, M.D.,	)	
COMMISSIONER	)	
OF FOOD AND DRUGS,	)	
et al.,	)	
	)	
Defendants.	)	

ORDER

This Court, having considered the decision of the United States Court of Appeals for the Federal Circuit, it is hereby ADJUDGED, ORDERED, AND DECLARED that:

1. Effective on the date of this Order, the expiration date for patent 3,927,046 will be November 19, 1995.

2. The Food and Drug Administration (FDA) shall publish the above patent expiration date in the "Orange Book."

3. The FDA is prohibited from approving any abbreviated new drug applications, abbreviated new animal drug applications, or applications filed pursuant to 21 U.S.C. § 355(b)(2) that do not take into account the patent expiration date for the above patent as determined by this Order.

/s/ Albert V. Bryan, Jr.
United States District Judge

Alexandria, Virginia
Date: 9/13/96

APPENDIX E

60 Federal Register 3398 (January 17, 1995)

Patent and Trademark Office

Notice of Hearing and Request for Comments on Changes to a Twenty-Year Patent Term and Its Effects on Patent Expiration Dates and Patent Term Extensions

AGENCY: Patent and Trademark Office, Commerce.

ACTION: Notice of public hearing and request for comments.

SUMMARY: In a Notice published on December 21, 1994 [59 FR 63951], the Patent and Trademark Office ("PTO") announced a public hearing on proposed changes related to the 20-year patent term contained in the Uruguay Round Agreements Act ("URAA"), Pub. L. 103-465.

Concurrently with the hearing scheduled for February 16, 1995, PTO also seeks comments on several additional issues that are relevant to the Food and Drug Administration's interpretation and application of current provisions of the Federal Food, Drug, and Cosmetic Act ("FDCA") and its implementing regulations in light of the changes to title 35, United States Code, effected by passage of the URAA. The specific provisions of the FDCA that would be affected govern the submission of

patent information related to new drug applications ("NDAs") and the submission and approval of abbreviated new drug applications ("ANDAs") for generic equivalents of listed drugs in anticipation of the expiration of patent protection for the listed drugs. (See 21 U.S.C. 321; 21 CFR part 314, subparts C and D.) Similarly affected may be FDCA provisions related to the submission of new animal drug applications ("NADAs") and the submission and approval of abbreviated new animal drug applications ("ANADAs"). (See 21 U.S.C. 360b). Because the changes to title 35 may affect the effective date of ANDA and ANADA approval under the FDCA and are relevant to the issues that will be discussed at the public hearing to be held on February 16, 1995, PTO will set aside a portion of the meeting to address these issues.

In addition, PTO seeks comments on the URAA's effect on existing patent term extensions under 35 U.S.C. 156.

DATES: The public hearing will be held on February 16, 1995, at 9:30 a.m. in the Commissioner's Conference Room 912, Crystal Park 2, 2121 Crystal Drive, Arlington, Virginia. Oral testimony on issues addressed in this notice will begin at 1:00 p.m. Requests to present oral testimony should be received on or before February 14, 1995. Written comments must be submitted on or before February 17, 1995.

ADDRESSES: Address written comments and requests to present oral testimony to the Commissioner of Patents and Trademarks, Washington, D.C. 20231. Attention: Stephen

G. Kunin, Deputy Assistant Commissioner for Patent Policy and Projects, Crystal Park 2, Suite 919, or by fax to (703) 305-8825. Persons with comments on the issues raised in this notice should also forward copies of those comments to the Food and Drug Administration, Attention: Dockets Management Branch (HFA-305), Room 1-23, 12420 Parklawn Dr., Rockville, MD 20857, identified with docket number 95N-0005.

FOR FURTHER INFORMATION CONTACT: H. Dieter Hoinkes by telephone at (703) 305-9300, by fax at (703) 305-8885, through electronic mail to hoinkes@uspto.gov, or by mail marked to his attention addressed to the Commissioner of Patents and Trademarks, Box 4, Washington, DC 20231. Persons may also contact Brain Malkin by Phone at (301) 443-1382, by fax at (301) 443-0232 or by mail marked to his attention and addressed to the Food and Drug Administration, Office of Health Affairs, HFY-20, 5600 Fishers Lane, Rockville, MD 20857.

SUPPLEMENTARY INFORMATION:

I. The Effect of URAA on the FDCA's ANDA Approval Process

Background

As described in detail in the Federal Register notice published on December 12, 1994, the URAA was signed into law on December 8, 1994 (Pub. L. 103-465). The amendments to title 35, United States Code, in the URAA

that relate to patent terms will become effective June 8, 1995. Certain provisions of the URAA patent amendments will change the term of existing patents from 17 years from the date of patent grant to 20 years from the date of filing of the patent application. If the patent application contains a specific reference to an earlier application under 35 U.S.C. 120, 121 or 365(c), the patent term will end 20 years from the date on which the earliest application relied on was filed. Patents that are in force on, or applied for by, June 8, 1995, will be entitled to the longer of 17 years from the date of the grant of the patent, or 20 years from the date of filing of the application. In addition, the URAA patent amendments provide for the extension of patents (up to a maximum of five years) in certain specified instances where there was delay in the issuance of the patent. This extension is separate from, and in addition to, the patent term extension available under 35 U.S.C. 156.

Section 532(c)(2) of the URAA patent amendments also limits the remedies available to a patent holder for patent infringement under certain circumstances. Specifically, a patent holder may not obtain an injunction or monetary damages, currently provided under title 35, for "acts which (A) were commenced or for which substantial investment was made before [June 8, 1995] and (B) became infringing by reason of [any amendment to a patent term resulting from the new 20-year provision]." Instead, the patent holder may only collect an "equitable remuneration" under such circumstances.

These amendments to title 35 may affect the drug approval process. Under the FDCA, pharmaceutical companies seeking to market pioneer drugs must first obtain FDA approval through the filing of an NDA (see, 21 U.S.C. 355(a) and (b)). In addition to data demonstrating the safety and effectiveness of the drug, an NDA applicant is required to submit to FDA information on any patent which claims the drug or a method of using such drug for which a claim of patent infringement could reasonably be asserted against an unauthorized party (see, 21 U.S.C. 355(b)(1) and (c)(2)). The patent information must include the patent number and date of expiration. FDA publishes this required information in its official publication, *Approved Drug Products With Therapeutic Equivalence Evaluations* (commonly referred to as the "Orange Book").

Under section 505(j)(2)(A)(vii) of the FDCA (21 U.S.C. 355 (j)(2)(A)(vii)), an ANDA must include a certification, in the opinion of the applicant and to the best of applicant's knowledge with respect to each patent which claims the listed drug, (I) that such patent information has not been filed, (II) that such patent has expired, (III) of the date on which such patent will expire, or (IV) that such patent is invalid or will not be infringed by the manufacture, use, or sale of the new drug for which the application is submitted. In addition, an ANDA applicant, who certifies that a patent is either invalid or will not be infringed, must provide notice of this filing to each owner of the patent as well as to the holder of the approved NDA for the listed drug which is claimed by the patent (see 21 U.S.C. 355(j)(2)(B)(i)). This notice must contain a

statement of the legal and factual grounds that support the applicant's opinion that the patent is not valid, unenforceable, or will not be infringed (see 21 U.S.C. 355(j)(2)(B)(ii); 21 CFR 314.52(c)(6)).

Under the FDCA, an ANDA approval shall be made effective on the date certified by the ANDA applicant to be the date on which a patent expires (see 21 U.S.C. 355(j)(4)(B)(ii)), or immediately if certified by the ANDA applicant (1) that patent information has not been filed or that the patent has expired (see 21 U.S.C. 355(j)(4)(B)(i)); or (2) that the patent is invalid or will not be infringed, unless an action is brought within 45 days after the ANDA applicant gives notice to the patent holder under section 5050(j)(2)(B)(i) of the FDCA (see 21 U.S.C. 355(j)(4)(B)(iii)).

The FDCA and implementing regulations provide no other mechanism by which to stay the effective date of an ANDA approval.

Under the FDCA, similar provisions apply to NADAs and ANADAs. Upon the approval of an NADA, FDA publishes required NADA patent information in its official publication, *FDA Approved Animal Drug Products* (referred to as the "Greek Book"). (See 21 U.S.C. 360b(b)(1)). ANADAs are subject to patent certification requirements (see 21 U.S.C. 360b(n)(1)(H)) and to approval effective dates (see 21 U.S.C. 360b(c)(2)(D)), similar to the ANDA provisions described above. The effective approval data of an ANADA, similar to an ANDA, is stayed only if an action is brought within 45

days after the ANADA applicant gives notice to the patent holder under 21 U.S.C. 360(n)(2)(B)(i), that the patent is not valid or will not be infringed. The FDCA provides no other mechanism by which to stay the effective date of an ANADA.

Issues Upon Which Comments Are Sought

Comments are requested regarding the effect of the URAA patent amendments upon the filing and approval of ANDAs and ANADAs. Specifically, comments are requested on the following questions:

1. Should FDA revised the patent term expiration dates currently listed in the Orange Book and Green Book for those patents entitled to a longer term under the URAA, because they are in force on June 8, 1995?

2. Should PTO, at the request of NDA or NADA holders, certify (or alternatively, verify) new patent expiration dates under the URAA for patents currently listed in the Orange Book and the Green Book?

3. Should NDA and NADA holders be required to submit to FDA revised patent expiration dates for those patents currently listed in the Orange Book and Green Book that will have a longer term under URAA? If so, should such submissions be required to be made (1) by June 8, 1995, (2) only after PTO certifies or verifies the claimed patent term expiration date, or (3) within some other specified time period?

4. If revised patent term expiration dates are published in the Orange Book and the Green Book, then if PTO does not certify or verify the patent term expiration date identified by the NDA or NADA holder, what submission, if any, should FDA require to verify the date? Should FDA publish the revised patent term expiration date submitted by the NDA or NADA holder without verification?

5. If revised patent term expiration dates are published in the Orange Book and the Green Book, what revisions to patent certification, if any, should applicants with pending ANDAs or ANADAs be required to make? When should such revisions to patent certifications be made? What type of information related to substantial investment, if any, should ANDA and ANADA applicants be required to make with such revisions?

II. The Effect of URAA on Existing Patent Term Extensions Under 35 U.S.C. 156

Under 35 U.S.C. 156, patent term extensions are issued for eligible patents from the original expiration date of the patent. Since this provision was enacted in 1984, the PTO has issued 195 certificates of patent term extension in accordance with section 156. Under the URAA, patents in force on June 8, 1995, are entitled to a patent term of 17 years from grant or 20 years from filing, whichever is longer. The PTO estimates that 93 patents whose terms were extended under section 156 would be entitled to such longer patent term. The PTO has assumed, for the purpose of evaluating the number of extending

patents that may be affected by the 20-year patent term, that a patent that would have expired (under the original 17-year patent term) before June 8, 1995, but has received a patent term extension for a period beyond June 8, 1995 (with the rights prescribed in 35 U.S.C. 156(b)), is a patent "in force" on June 8, 1995.

There are several ways to interpret the provision of the URAA that grants the longer of a 17 or 20-year patent term to patents in force on June 8, 1995, and that have been or will be extended under section 156. First, the extension already issued by the PTO could simply be added to the longer of the 17 or 20-year patent term. No action would be required by the PTO. Second the extension already issued by the PTO could be interpreted to operate from "the original expiration date of the patent" (35 U.S.C. 156(a)), which could be interpreted as the expiration date of the 17-year patent term. Again, no action would be required by the PTO. A third interpretation could be that the appropriate extension under section 156 would be added to the longer of the 17 or 20-year patent term. This third interpretation would require the PTO to revise the extension granted in some cases as the 14-year limitation of a patent term counted from the date of market approval (35 U.S.C. 156(c)(3)) would be applicable to the extended patent term regardless of whether the original expiration date of the patent was 17 years from grant or 20 years from the filing date. The PTO seeks comments from the public on the appropriate course of action with respect to patents that have been or will be issued term extensions under section 156 of title 35, United States Code.

Questions

1. Should PTO take any action with respect to existing patent term extensions under section 156?

2. What approach should PTO take with respect to the calculation of new patent term extensions under section 156 where the patent is entitled to the longer of the 17 or 20-year patent term under the URAA?

Comments on any other issues relevant to the relationship between the URAA and the FDCA or existing patent term extensions under 35 U.S.C. 156 are also invited.

Dated: January 11, 1995.

Michael K. Kirk,
Deputy Assistant Secretary of Commerce and Deputy Commissioner of Patents and Trademarks.

[FR Doc. 95-1073 Filed 1-13-95; 8:45 am]

BILLING CODE 3510-16-M

APPENDIX F

60 Federal Register 15748 (March 27, 1995)

Patent and Trademark Office

Proposed Determination of New Expiration Dates of Certain Patents

AGENCY: Patent and Trademark Office, Commerce.

ACTION: Request for comments.

SUMMARY: The Patent and Trademark Office (PTO) intends to determine and publish the new expiration dates of patents that, (1) are in force on June 8, 1995, (2) are entitled to a term of 20 years from filing, and (3) have received a term extension under either section 155 or 156 of title 35, United States Code. The PTO seeks written comments on its intended course of action.

DATES: Written comments must be submitted on or before April 26, 1995

ADDRESSES: Address written comments to the Commissioner of Patents and Trademarks, Washington, DC 20231, Attention: H. Dieter Hoinkes, Office of Legislative and International Affairs, Crystal Park 2, Suite 902, or by facsimile to (703) 305-3885.

FOR FURTHER INFORMATION CONTACT: H. Dieter Hoinkes by telephone at (703) 305-9300, by facsimile at (703) 305-8885, or by mail marked to his attention addressed to the Commissioner of Patents and Trademarks, Box 4, Washington, DC 20231.

SUPPLEMENTARY INFORMATION: Under section 156 of title 35, United States Code, patent term extensions are issued for eligible patents from the original expiration date of the patent. Since this provision was enacted in 1984, the PTO has issued 195 certificates of patent term extension in accordance with section 156. Under the Uruguay Round Agreements Act ("URAA"), Public Law 103-465, patents in force on June 8, 1995, are entitled to a patent term of 17 years from grant or 20 years from their earliest filing date, whichever is greater (see 35 U.S.C. 154(c)(1)). It is estimated that 94 patents whose terms were extended under section 156 are entitled to such a longer patent term.

On February 16, 1995, the PTO held a public hearing to elicit comments on what action it should take regarding patents that are entitled to a longer patent term under the URAA and that had previously been extended under section 156. (See 60 Fed. Reg. 3398 (Jan. 17, 1995)). After having considered all the comments, both written and oral, the PTO intends to publish the new expiration date of all patents that fall into the category mentioned above. The determination of the new expiration dates will be based on the following three considerations:

(1) A patent that would have expired under the original 17-year patent term before June 8, 1995, but that has received a patent term extension for a period beyond June 8, 1995, is a patent "in force" on June 8, 1995, even though the rights derived from that patent are circumscribed by section 156(b) of title 35.

(2) The "original expiration date of the patent" referred to in section 156(a) of title 35 is the date on which the patent would have expired if it had not been extended under section 156 to expire at a later date. Therefore, the "original expiration date" of the patents under consideration is the date on which the 20-year term from filing terminates.

(3) The extension already issued on the basis of the 17-year term will be added to the 20-year term, subject to the limitation imposed by section 156(c)(3) of title 35. That provision limits the period remaining in the term of an extended patent to fourteen years counted from the date on which the product under review received approval for commercial marketing by the relevant regulatory authority.

In addition, it should be noted that under the provisions of section 155 of title 35, 33 patents were extended, each for a period of five years, ten months and 17 days. Of the 32 patents in force on June 8, 1995, 20 are entitled to the longer term of 20 years from their relevant filing date. Their new expiration date, taking into account the term of extension provided by 35 U.S.C. 155, is also intended to be published.

Comments are invited on the course of action the PTO intends to undertake with respect to the new expiration dates of patents in the category discussed above. In issuing its final determination, the PTO will respond to significant comments received.

Dated: March 20, 1995.

Bruce A. Lehman,
Assistant Secretary of Commerce and Commissioner of Patents and Trademarks.

[FR Doc. 95-7388 Filed 3-24-95; 8:45 am]

Billing Code 3510-16M

APPENDIX G

60 Federal Register 30069 (June 7, 1995)

Patent and Trademark Office

Determination of New Expiration Dates of Certain Patents

AGENCY: Patent and Trademark Office, Commerce.

ACTION: final Determination.

SUMMARY: The Patent and Trademark Office (PTO) has determined the expiration date of patents that:

(1) Are in force on June 8, 1995, and, therefore, are entered to the greater of a term of 20 years from their relevant filing date, or 17 years from grant, and

(2) Have received a term extension under section 155 or 156 of title 35, United States Code, or will receive a term extension under section 156 in the future.

All patents falling in this category are entitled to the longer term of either (a) 17 years from grant, supplemented by the period of extension obtained under section 155 or 156, or (b) 20 years from their relevant filing date.

FOR FURTHER INFORMATION CONTACT: H. Dieter Hoinkes, by telephone at (703) 305-9300, by facsimile at (703) 305-8885, or by mail marked to his attention addressed to the Commissioner of Patents and Trademarks, Box 4, Washington, DC 20231.

SUPPLEMENTARY INFORMATION: Under section 156 of title 35, United States Code, patent term extensions are issued for eligible patents from the original expiration date of the patent. Since this provision was enacted in 1984, the PTO has issued 195 certificates of patent term extension in accordance with section 156. Under the Uruguay Round Agreements Act ("URAA"), Public Law 103-465, patents in force on June 8, 1995, are entitled to a patent term of 17 years from grant or 20 years from their earliest filing date, whichever is greater (See 35 U.S.C. 154(c)(1)).

On February 16, 1995, the PTO held a public hearing to elicit comments on what action it should take regarding patents that are entitled to a longer patent term under the URAA and that had previously been extended under section 156. (See 60 FR 3398 (Jan. 17, 1995)). After having considered all the comments, both written and oral, the PTO requested public comments on its intent to publish the new expiration date of all patents that fall into the category mentioned above (See 60 FR 15748 (March 27, 1995)), using the following three criteria:

(1) A patent that would have expired under the original 17-year patent term before June 8, 1995, but that has received a patent term extension for a period beyond

June 8, 1995, is a patent "in force" on June 8, 1995, even though the rights derived from that patent are circumscribed by section 156(b) of title 35.

(2) The "original expiration date of the patent" referred to in section 156(a) of title 35 is the date on which the patent would have expired if it had not been extended under section 156 to expire at a later date. Therefore, the "original expiration date" of the patents under consideration is the date on which the 20-year term from filing expires.

(3) The extension already issued on the basis of the 17-year term is added to the 20-year term, subject to the limitation by imposed by section 156(c)(3) of title 35. That provision limits the period remaining in the term of an extended patent to fourteen years counted from the date on which the product under review received approval for commercial marketing by the relevant regulatory authority.

After analyzing the written comments received regarding the PTO's proposed intent to determine the expiration dates of the relevant patents, taking into account the three criteria noted above, it has been concluded that criterion (2) is in error and that, therefore, the steps outlined in criterion (3) are not an appropriate course of action. The provisions of section 156 cannot be applied *in vacuo* without obtaining results that could not have been intended by the URAA or that are inconsistent with section 156 itself.

The entire argument in favor of adding an extension obtained under section 156 to a 20-year term obtained under the URAA, was the manner of interpreting the provision in section 156(a), requiring that the term of a patent be extended from its "original expiration date". The term "original expiration date was proposed to be the date of a patent's expiration without the aid of an extension period, which was proposed to be the end of the 20-year term for those patents entitled to such term.

This narrow interpretation of section 156, however, did not take into account that the term "original" has several meanings, all of which must be taken into consideration to avoid an improper interpretation of the relationship between section 154(c)(1), added to title 35 by the URAA, and section 156, enacted in 1984. To that end, considering the expiration of the longer 20-year term to be the original expiration date, ignores the fact that when the patent was issued, it originally had an expiration date of 17 years from grant. That date must continue to be considered "original" for two reasons.

One is, that this was the date on which the patent, when granted, was set to expire. Accordingly, if a patent is now entitled to a longer 20-year term, such is merely an added time period beyond the original expiration date. The other reason is the impossibility of having more than one "original expiration date" without having to refer to one as the first "original" and to the other as the second or new "original", the latter being a contradiction in terms.

Had criteria (2) and (3) been adopted, additional anomalies would have arisen. For example, the term "original expiration date" means the date on which a patent would have expired without the extension added by section 156. In the case of many patents in question, their being in force on June 8, 1995, and their entitlement, therefore, to the longer term of 20 years from filing, was solely due to an extension of the original patent term under section 156. In other words, their entitlement to a 20-year term rests on a patent term extension. It is not reasonable, therefore, to ascribe to the end of such 20-year term the appellation "original expiration" which under the provisions of section 156(a) was supposed to have been achieved without the aid of an extended term.

Moreover, in cases where the 17-year term expires before June 8, 1995, and the patent is kept in force on that date by virtue of an extension under section 156, transposing such extension to the end of the 20-year term would have resulted in applying at least some of the extended period twice to the term of the patent. This result would have been especially curious in instances where both the original 17 and the 20-year terms expired before June 8, 1995.

Another vexing problem that would have arisen had the PTO proposal been adopted, concerns the question of the rights that a patent holder derives during the period of extension under section 156. If this period had been added to the 20-year term, a patentee would have had full exclusionary rights until the end of the 17-year term, followed by rights only to equitable remuneration with

respect to a certain class of infringers during the period from the end of the 17-year term to the end of the 20-year term, and followed by a restoration of full exclusionary rights with respect to the approved product during the continuing period of extension under section 156. A more reasonable solution, such as a continuation of limited patent rights during the period of extension, has no statutory foundation, because section 154(c)(2) added by the URAA does not address extensions under section 156, which itself contains an explicit provision regarding a patentee's rights during the period of extension.

In analyzing section 156(a), it must be remembered that at the time of its enactment in 1984, only one patent term--seventeen years from grant--was available and that all extensions granted under section 156 until now were added to that patent term. Because the URAA does not address the question of patent term extension under section 156, the extensions of all patents issued before June 8, 1995, must continue to be calculated by the PTO on the basis of the 17-year term from grant and added to that term. This is necessitated by the fact that all patents in that category have an original expiration of 17 years from grant, even though they may be entitled to a term of 20 years from filing under the URAA. Further, where the 20-year term from filing exceeds the original term of 17 years from grant, the provisions of the URAA are satisfied in cases where the extension under section 156, added to the 17-year term, expires later than 20 years from the filing date.

All patents in force on June 8, 1995, were originally issued with a term of 17 years from grant. The fact that on June 8, 1995, these patents are entitled to a term of 20 years from filing, if that term exceeds the 17-year term, does not move the original expiration date from which a period of extension continues, if granted under section 156. It only provides a new--albeit not original--expiration date. Accordingly, all patents in this category are entitled either to the 17-year term, as augmented by an extension under section 156, or to a 20-year term from the relevant filing date, whichever is longer. This determination is fully consistent with section 154(c)(1) of title 35, as added by the URAA, because extensions under section 156 are not addressed by section 154(c)(1) and are, therefore, left untouched.

Of course, all patents issued after June 8, 1995, on applications filed before that date, are also entitled to a term that is the greater of 17 years from grant or 20 years from their relevant filing date. Extensions under section 156 granted to these patents must be calculated with reference to whatever term is applicable at their time of issue and will then be added to that term. As these patents have only one term at issue, there is no question regarding their original expiration date.

Further, under the provisions of section 155 of title 35, 33 patents were extended, each for a length of time to be measured from the date a "stay of regulation of approval was imposed" (December 5, 1975) to the date commercial marketing was permitted (October 22, 1981). This time period amounts to 2,148 days. One of these 33

patents expired in 1992, leaving 32 in force on June 8, 1995.

Section 155 differs from section 156 in providing that "the term of a patent * * * shall be extended * * * by a length of time * * *", rather than that the term of a patent shall be extended "from the original expiration date." This difference, however, has no practical effect because the 33 patents that originally were eligible for extension under section 155 already have been extended, as required by that provision. The provisions of section 154(c)(1), therefore, would only have had an effect, if the 20-year term to which 21 patents are entitled, exceeded the 17-year patent term, as extended by 2,148 days. Applying the provisions of section 154(c)(1) to these patents, however, reveals that its requirements are already satisfied, because all previously extended terms exceed a term of 20 years from the patents' relevant filing dates. Accordingly, section 154(c)(1) does not benefit any of the patents already extended under section 155.

Comments

Nine written comments were received in response to PTO's request for comments mentioned above. Responses to significant comments follow.

1. Comment: One comment urged that any period of patent term extension used to keep a patent in force on June 8, 1995, not be added to the 20-year term and that only the portion of the extended patent term past June 8, 1995, be added.

Response: The suggestion has not been adopted because neither section 156 of title 35, nor section 154(c)(1), as added by the URAA, contains a provision that would permit apportioning a term of patent extension in the manner suggested.

2. *Comment*: Two comments suggested that all patents that received an extension under section 156 prior to June 8, 1995, were extended from an "original expiration date" and that neither the URAA nor section 156 authorizes any alteration. It was suggested, therefore, that any patent in force on June 8, 1995, should expire either at the end of the term extension under section 156 as added to the 17-year term, or at the end of 20 years from filing, whichever is longer.

Response: The suggestion has been adopted for the reasons given above.

3. *Comment*: Four comments endorsed the PTO's proposal to move the term of extension from the original expiration date of the patent to its new expiration date, although two of the comments took issue with the proposal that the period of extension comply with the limitation proposed by section 156(c)(3).

Response: In light of the fact that the original PTO proposal has not been followed, the question of the applicability of section 156(c)(3) is moot. Nevertheless, it appears anomalous that some supporters of the original PTO proposal would have looked to section 156 for support of transposing the period of extension, while

disclaiming the validity of other provisions in section 156 that materially affect that extension.

4. Comment: One comment suggested that the PTO certify the new patent expiration date upon the patentee's request.

Response: The suggestion has not been adopted, as this final determination of the expiration dates of the relevant patents makes certification unnecessary.

It should be noted that any patent in force on June 8, 1995, and any patent issued on the basis of an application filed before June 8, 1995, are entitled to the longer term of 17 years from grant or 20 years from the relevant filing date. Because patents issued before June 8, 1995, were initially given a term of 17 years from grant, any extension under section 156 must begin from the original expiration date, which is the end of the 17-year term. If the term of 20 years from the relevant filing date exceeds the expiration of the extended term, the patent is entitled to such later expiration date. Patents issued after June 8, 1995, on the basis of applications filed before such date, are also entitled to the greater one of the two terms mentioned above. However, as this term attaches at the time of issue, the question of what term is extended under section 156 does not arise.

As the information to determine the applicable expiration dates of all these patents is readily available from relevant patent documents, publication of their

expiration dates is not necessary for the purpose of clarification.

Dated: June 1, 1995.

Bruce A. Lehman,
Assistant Secretary of Commerce and Commissioner of Patents and Trademarks.

[FR Doc. 95-13848 Filed 6-2-95; 1:42 pm]

BILLING CODE 3510-16-M

APPENDIX H

60 Federal Register 30309 (June 8, 1995)

Food and Drug Administration

[Docket Nos. 95P-0061, 95S-0117, 95S-0126, and 95S-0135]

Patent Term Extensions Under the Uruguay Round Agreements Act and Their Effects on Marketing Applications for Human and Animal Drug Products

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of availability.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of its response to a citizen petition from Glaxo Pharmaceuticals, Inc. (Glaxo). The petition requested that the agency announce how the Uruguay Round Agreements Act (URAA) will affect the patent information submission and patent certification requirements for applications to market drug products under the Federal Food, Drug, and Cosmetic Act (the act). FDA responded to the petition on May 25, 1995. The response provides applicants with current information on how the URAA will affect patent term extension requirements for applications to market human and animal drugs.

DATES: Amended patent information, reflecting any extended patent terms under the URAA, should be submitted to FDA before July 8, 1995, but no earlier than June 8, 1995.

ADDRESSES: Copies of the citizen petition (95-P0061/CP1), comments submitted to FDA regarding the citizen petition, and FDA's response to the citizen petition may be obtained from the Freedom of Information Staff (HFI-35), Food and Drug Administration, rm. 12A-16, 5600 Fishers Lane, Rockville, Md. 20857. Copies are also available for public examination of the Dockets Management Branch (HFA-305), Food and Drug Administration, rm. 1-23, 12420 Parklawn Dr., Rockville, Md. 20857, between 9 a.m. and 4 p.m., Monday through Friday.

FOR FURTHER INFORMATION CONTACT: Wayne H. Mitchell, Center for Drug Evaluation and Research (HFD-362), Food and Drug Administration, 7500 Standish Place, Rockville, Maryland 20855, 301-594-1049.

SUPPLEMENTARY INFORMATION: On December 8, 1994, the URAA (Pub. L. 103-465) was signed into law. The URAA made amendments to Title 35 of the United States Code. These amendments relate to patent terms for existing and future patents, and they will become effective on June 8, 1995. Certain provisions of the URAA patent amendments will change the terms of some existing patents from 17 years from the date of the granting of the patent to 20 years from the filing of the patent application.

On February 16, 1995, the Patent and Trademark Office (PTO) held a public hearing on the patent provisions amended by the URAA. The PTO devoted a portion of the hearing to addressing several issues pertaining to the effect of these changes in patent law on FDA's enforcement of the act. (See the **Federal Register** notice of January 17, 1995 (60 FR 3398).) Oral testimony was given at the hearing and written submissions were made to PTO and FDA. Glaxo submitted its citizen petition to FDA on March 7, 1995. The petition requested that the agency announce the effect the URAA will have on the patent information submission and patent certification requirements for applicants to market drug products under the act. FDA has received a number of responses to Glaxo's citizen petition from generic and innovator drug manufacturers. Glaxo submitted an additional comment on the responses dated April 13, 1995. These documents are included in Docket No. 95P-0061. These oral and written submissions were considered by FDA in developing its response to the petition.

A brief summary of FDA's position on patent term extensions under the URAA is set out below in this document. A fuller exposition of the agency's position may be found in the response to Glaxo's petition.

I. Submission of Patent Information

FDA has determined that if the patent term expiration date for a listed human or animal drug product is extended by the URAA, the new drug application (NDA) or new animal drug application (NADA) holder

must submit information and the new patent term expiration date to FDA after June 8, 1995, but before July 8, 1995. NDA holders who have already submitted information indicating that listed patents will be extended by the URAA should resubmit this information on or after June 8, 1995.

Two copies of amended patent information pertaining to human drug products regulated under section 505 of the act (21 U.S.C. 355) by the Center for Drug Evaluation and Research (CDER) should be submitted to the assigned reviewing division. The submission should bear the pertinent NDA number. Two copies of the amended patent information pertaining to human drug products regulated under section 505 of the act by the Center for Biologics Evaluation and Research (CBER) should be sent to the Document Control Center, Center for Biologics Evaluation and Research (HFM-99), Food and Drug Administration, 1401 Rockville Pike, suite 200N, Rockville, MD 20852-1448.

To expedite the availability to the public of the updated patent information, a third copy of the amended patent information pertaining to human drug products regulated under section 505 of the act by either CDER or CBER should be sent to the Drug Information Services Branch, Center for Drug Evaluation and Research, Food and Drug Administration (HFD-84), 5600 Fishers Lane, Rockville, MD 20857.

Amended patent information pertaining to animal drug products should be sent to the Document Control

Unit, Center for Veterinary Medicine (HFV-199), Food and Drug Administration, 7500 Standish Pl., Rockville, Md. 20855.

II. Public Availability of Updated Patent Information

Updated information related to patents on human drug products regulated by CDER will be placed on public display in thee Dockets Management Branch (address above) under Docket No. 95S-0117, after June 8, 1995. Updated information related to patents on human drug products regulated by CBER will be placed on public display in the Dockets Management Branch under Docket No. 95S-0135. Updated information related to patents on animal drug products will be placed on public display in the Dockets Management Branch under Docket No. 95S-0126. Updated patent information for human drug products will be published in the monthly supplements to "Approved Drug Products with Therapeutic Equivalence Evaluations" (the Orange Book) and updated patent information for animal drug products will be published in the monthly supplements to "FDA Approved Animal Drug Products" (the Green Book) after June 8, 1995.

III. Amended Patent Certifications

Abbreviated new drug applications (ANDA's), abbreviated new animal drug applications (ANADA's), and applications provided for in section 505(b)(2) of the act (505(b)(2) applications) pending before the agency on June 8, 1995, including such applications that may have

received tentative approval letters, must be amended to respond to the URAA-extended patent expiration dates, if information on the new expiration dates is submitted to the agency of the NDA or NADA holder in a timely manner. ANDA's, ANADA's, and 505(b)(2) applications submitted after June 8, 1995, likewise must provide patent certifications with respect to the URAA-extended patent expiration dates. After June 8, 1995, FDA will not approve any application that does not contain a correct certification with respect to a URAA-extended patent expiration date that was submitted in a timely manner to the agency. The agency expects that an application that wishes to market a drug under an approved ANDA, ANADA, or 505(b)(2) application before the expiration of a URAA-extended patent, for which information was submitted to FDA in a timely manner, will file a paragraph IV certification with respect to that patent (See sections 505(b)(2)(A), (j)(2)(A)(vii), and 512(n)(1)(H) of the act.)

Amended patent certification statements for abbreviated new drug applications (ANDA's) and 505(b)(2) applications reviewed by the Office of Generic Drugs should be sent to the Office of Generic Drugs, Center for Drug Evaluation and Research (HFD-600), Food and Drug Administration, 7500 Standish Pl., Rockville, MD. 20855. Amended patent certification statements for 505(b)(2) applications reviewed by the new drug reviewing divisions within CDER should be sent to the appropriate review division. Amended patent certification statements pertaining to animal drug products should be sent to the Document Control Unit, Center for Veterinary Medicine (HFV-199), Food and Drug Administration, 7500 Standish

Pl., Rockville, Md. 20855. Amended patent certification statements pertaining to biological products should be sent to the Document Control Center, Center for Biologics Evaluation and Research (HFM-99), Food and Drug Administration, 1401 Rockville Pike, suite 200N, Rockville, Md. 20852-1448.

Dated: June 2, 1995

William B. Schultz,
Deputy Commissioner for Policy.

[FR Doc. 95-14040 Filed 6-5-95; 2:29 pm]

Billing Code 4160-01-F

APPENDIX I

60 Federal Register 37652 (July 21, 1995)

[Docket Nos. 95P-0061, 95S-0117, 95S-0126, and 95S-0135]

Patent Term Expiration Dates for Patents Extended by the Uruguay Round Agreements Act; Submission by Applications of New Drug and New Animal Drug Applications

AGENCY: Food and Drug Administration, HHS.

ACTION Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing its position on patent information submitted by applicants of new drug applications (NDA's) and new animal drug applications (NADA's). Patent term expiration dates for certain patents that are subject to both the Uruguay Round Agreements Act (URAA) and the patent term extension provisions of the United States Code should be calculated in accordance with the Patent and Trademark Office's (PTO's) determination of June 7, 1995. FDA will not publish dates that the NDA or NADA applicant states are not calculated in accordance with the June 7, 1995, determination. This document is intended to advise all NDA and NADA applicants who submitted URAA-extended patent term expiration dates that were not

calculated in accordance with the PTO's determination to submit correct patent term expiration dates to the agency.

DATES: NDA and NADA applicants that submitted inaccurate patent term expiration dates should submit patent term expiration dates calculated in accordance with the PTO's determination by August 21, 1995.

ADDRESSES: Two copies of amended patent information pertaining to human drug products regulated under section 505 of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 355) by CDER should be submitted to the assigned reviewing division. The submission should bear the pertinent NDA number.

Two copies of amended patent information pertaining to human drug products regulated under section 505 of the act by CBER should be submitted to the Document Control Center, Center for Biologics Evaluation and Research (HFM-99), Food and Drug Administration, suite 200N, Rockville, MD 20852.

A third copy of the amended patent information pertaining to human drug products regulated under section 505 of the act by either the Center for Drug Evaluation and Research (CDER) or the Center for Biologics Evaluation and Research (CBER) should be sent to the Division of Drug Information Services (HFD-85), Center for Drug Evaluation and Research, Food and Drug Administration, 1901 Chapman Ave., rm. 212, Rockville, MD 20852.

Amended patent information pertaining to animal drug products should be sent to the Document Control Unit, Center for Veterinary Medicine (HFV-199), Food and Drug Administration, 7500 Standish Pl., Rockville, MD 20855.

FOR FURTHER INFORMATION CONTACT: Wayne H. Mitchell, Center for Drug Evaluation and Research (HFD-362), Food and Drug Administration, 7500 Standish Pl., Rockville, MD 20855, 301-594-1049.

SUPPLEMENTARY INFORMATION: In the **Federal Register** of June 8, 1995 (60 FR 30309), FDA announced the availability of the agency's response to a citizen petition from Glaxo, Inc., requesting that FDA explain how the URAA affects the patent information submission and patent certification requirements for applications to market drug products under the act. In that notice, FDA directed that amended patent information, reflecting extended patent term expiration dates under the URAA, by submitted to FDA between June 8 and July 8, 1995.

On June 7, 1995, the PTO published a notice in the **Federal Register** (60 FR 30069) entitled "Determination of New Expiration Dates of Certain Patents" (the PTO's determination) that established the method of calculating the patent term expiration date for any patent subject to both the terms of the URAA and the patent term extension provisions at 35 U.S.C. 156. FDA has received from several NDA or NADA applicants submissions of new patent term expiration dates which the applicant submitting the information states were not calculated in accordance

with the PTO's determination. In order to comply with the requirements of sections 505(b) and 512(b) (21 U.S.C. 360(b)) of the act and 21 CFR 314.53, NDA and NADA applicants must submit accurate patent information. For the expiration dates for patents that received patent term extension under the URAA to be accurate, those dates must be calculated in accordance with the PTO's determination.

FDA is advising all NDA and NADA applicants who submitted URAA-extended patent term expiration dates that were not calculated in accordance with the PTO's determination to submit corrected patent term expiration dates to the agency by August 21, 1995. If the applicant has already submitted patent expiration dates that are consistent with the PTO's determination, no addition submission is necessary. FDA will not verify the patent expiration dates submitted by NDA and NADA applicants. FDA will not publish any patent expiration date that the submitter states is not consistent with the PTO's determination.

The agency will publish the new patent term expiration dates submitted during the June 8 to July 8, 1995, period that are not expressly identified by the applicant submitting the information as having been calculated in a manner inconsistent with the PTO's determination. FDA anticipates that the procedures set out in § 314.53(f) will govern with respect to challenges by third parties that the submitted patent term expiration date was not calculated in accordance with the PTO's determination. For these challenges, the procedures set out

in § 314.53(f) will be modified so that, if the applicant submitting the challenged patent term expiration date fails to notify FDA within 30 days of receiving notification from the agency of a challenge to the patent that the submitted date is consistent with the PTO's determination, FDA will not continue to publish the challenged date.

Two copies of amended patent information pertaining to human drug products regulated under section 505 of the act by CDER should be submitted to the assigned reviewing division. The submission should bear the pertinent NDA number.

Two copies of amended patent information pertaining to human drug products regulated under section 505 of the act by CBER should be submitted to the Document Control Center, Center for Biologics Evaluation and Research (HFM-99), Food and Drug Administration, suite 200N, Rockville, MD 20852.

To expedite the availability to the public of the undated patent information, a third copy of the amended patent information pertaining to human drug products regulated under section 505 of the act by either CDER or CBER should be sent to the Division of Drug Information Services (HFD-85), Center for Drug Evaluation and Research, Food and Drug Administration, 1901 Chapman Ave., rm. 212, Rockville, MD 20852.

Amended patent information pertaining to animal drug products should be sent to the Document Control Unit, Center for Veterinary Medicine (HFV-199), Food and

Drug Administration, 7500 Standish Pl., Rockville, MD 20855.

Dated: July 18, 1995.

William B. Schultz,
Deputy Commissioner for Policy.

[FR Doc. 95-18079 File 7-19-95; 11:00 am]

BILLING CODE 4160-01-F

APPENDIX J

United States Court of Appeals
for the Federal Circuit

96-1068, -1105, -1107

MERCK & CO., INC, AND MSD TECHNOLOGY, L.P.,

Plaintiffs-Appellees,

and

SCHERING CORPORATION,

Plaintiff-Appellee,

and

BRACCO DIAGNOSTICS INC. and
BRACCO INTERNATIONAL B.V.,

Plaintiffs-Appellees,

and

HOFFMANN-LA ROCHE INC. and
SYNTEX (U.S.A.) INC.,

Plaintiffs-Appellees,

and

ORGANON, INC.,

Plaintiff-Appellee,

v.

DAVID A. KESSLER, M.D.,
Commissioner of Food and Drugs, and
BRUCE A. LEHMAN, Assistant Secretary
of Commerce and
Commissioner of Patents and Trademarks,

Defendants-Appellants,

and

GENERIC PHARMACEUTICAL
INDUSTRY ASSOCIATION,

Defendant-Appellant.

ORDER

United States Court of Appeals
for the Federal Circuit

ORDER

A combined petition for rehearing and suggestion for rehearing in banc having been filed by APPELLEE Organon, and the petition for rehearing having been referred to the panel that heard the appeal, and thereafter the suggestion for rehearing in banc having been referred to the circuit judges who are in regular active service,

UPON CONSIDERATION THEREOF, it is

ORDERED that the petition for rehearing be, and the same hereby is, DENIED and it is further

ORDERED that the suggestion for rehearing in banc be, and the same hereby is, DECLINED.

The mandate of the court will issue on July 19, 1996.

Circuit Judge SCHALL did not participate in the vote.

FOR THE COURT
FRANCIS X. GINDHART, CLERK

Dated: July 12, 1996

By_____
Brian P. LeDuc
Associate Chief Deputy Clerk

cc: REUBEN ROBERTSON III, JOHN HOYLE
JOHN LYNCH, ROGER CLARK, DONALD BEERS
HARRIS WEINSTEIN, WAYNE MATELSKI
STONE, TSIEN, HITCHCOCK, COBRIN,
ARMITAGE

MERCK & CO V KESSLER, 96-1068, -1105, -1107
(DCT- 95-CV-1005)

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* *
* NOTE: Pursuant to Fed. Cir. R. 47.6, this order *
* is not citable as precedent. It is a public record. *
* *
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APPENDIX K

United States Court of Appeals
for the Federal Circuit

96-1068, -1105, -1107

MERCK & CO., INC, AND MSD TECHNOLOGY, L.P.,

Plaintiffs-Appellees,

and

SCHERING CORPORATION,

Plaintiff-Appellee,

and

BRACCO DIAGNOSTICS INC. and
BRACCO INTERNATIONAL B.V.,

Plaintiffs-Appellees,

and

HOFFMANN-LA ROCHE INC. and
SYNTEX (U.S.A.) INC.,

Plaintiffs-Appellees,

and

ORGANON, INC.,

Plaintiff-Appellee,

v.

DAVID A. KESSLER, M.D.,
Commissioner of Food and Drugs, and
BRUCE A. LEHMAN, Assistant Secretary
of Commerce and
Commissioner of Patents and Trademarks,

Defendants-Appellants,

and

GENERIC PHARMACEUTICAL
INDUSTRY ASSOCIATION,

Defendant-Appellant.

O R D E R

NOTE: Pursuant to Fed. Cir. R. 47.6, this order is not citable as precedent. It is a public record.

United States Court of Appeals
for the Federal Circuit

ORDER

A combined petition for rehearing and suggestion for rehearing in banc having been filed by APPELLEE Bracco, and responses thereto having been invited by the court and filed by various other parties, and the petition for rehearing having been referred to the panel that heard the appeal, and thereafter the suggestion for rehearing in banc and responses having been referred to the circuit judges who are in regular active service,

UPON CONSIDERATION THEREOF, it is

ORDERED that the petition for rehearing be, and the same hereby is, DENIED and it is further

ORDERED that the suggestion for rehearing in banc be, and the same hereby is, DECLINED.

The mandate of the court will issue on July 19, 1996.

Circuit Judge SCHALL did not participate in the vote.

FOR THE COURT
FRANCIS X. GINDHART, CLERK

Dated: July 12, 1996

By_____
Diane M. Frye
Chief Deputy Clerk

cc: R. ROBERTSON III, J. HOYLE, J. LYNCH,
R. CLARK, D. BEERS, H. WEINSTEIN,
W. MATELSKI, D. STONE, A TSIEN,
C. HITCHCOCK, P. COBRIN, R. ARMITAGE

MERCK & CO V KESSLER, 96-1068, -1105, -1107
(DCT- 95-CV-1005)

APPENDIX L

United States Court of Appeals
for the Federal Circuit

96-1068, -1105, -1107

MERCK & CO., INC, AND MSD TECHNOLOGY, L.P.,

Plaintiffs-Appellees,

and

SCHERING CORPORATION,

Plaintiff-Appellee,

and

BRACCO DIAGNOSTICS INC. and
BRACCO INTERNATIONAL B.V.,

Plaintiffs-Appellees,

and

HOFFMANN-LA ROCHE INC. and
SYNTEX (U.S.A.) INC.,

Plaintiffs-Appellees,

and

ORGANON, INC.,

Plaintiff-Appellee,

v.

DAVID A. KESSLER, M.D.,
Commissioner of Food and Drugs, and
BRUCE A. LEHMAN, Assistant Secretary
of Commerce and
Commissioner of Patents and Trademarks,

Defendants-Appellants,

and

GENERIC PHARMACEUTICAL
INDUSTRY ASSOCIATION,

Defendant-Appellant.

ORDER

NOTE: Pursuant to Fed. Cir. R. 47.6, this order is not citable as precedent. It is a public record.

United States Court of Appeals
for the Federal Circuit

ORDER

A combined petition for rehearing and suggestion for rehearing in banc having been filed by APPELLANT Kessler, and responses thereto having been invited by the court and filed by various other parties, and the petition for rehearing having been referred to the panel that heard the appeal, and thereafter the suggestion for rehearing in banc and responses having been referred to the circuit judges who are in regular active service,

UPON CONSIDERATION THEREOF, it is

ORDERED that the petition for rehearing be, and the same hereby is, DENIED and it is further

ORDERED that the suggestion for rehearing in banc be, and the same hereby is, DECLINED.

The mandate of the court will issue on July 19, 1996.

Circuit Judge SCHALL did not participate in the vote.

FOR THE COURT
FRANCIS X. GINDHART, CLERK

Dated: July 12, 1996

By_____
Diane M. Frye
Chief Deputy Clerk

cc: R. ROBERTSON III, J. HOYLE, J. LYNCH,
R. CLARK, D. BEERS, H. WEINSTEIN,
W. MATELSKI, D. STONE, A TSIEN,
C. HITCHCOCK, P. COBRIN, R. ARMITAGE

MERCK & CO V KESSLER, 96-1068, -1105, -1107
(DCT- 95-CV-1005)

APPENDIX M

United States Court of Appeals
for the Federal Circuit

96-1068, -1105, -1107

MERCK & CO., INC, AND MSD TECHNOLOGY, L.P.,

Plaintiffs-Appellees,

and

SCHERING CORPORATION,

Plaintiff-Appellee,

and

BRACCO DIAGNOSTICS INC. and
BRACCO INTERNATIONAL B.V.,

Plaintiffs-Appellees,

and

HOFFMANN-LA ROCHE INC. and
SYNTEX (U.S.A.) INC.,

Plaintiffs-Appellees,

and

ORGANON, INC.,

Plaintiff-Appellee,

v.

DAVID A. KESSLER, M.D.,
Commissioner of Food and Drugs, and
BRUCE A. LEHMAN, Assistant Secretary
of Commerce and
Commissioner of Patents and Trademarks,

Defendants-Appellants,

and

GENERIC PHARMACEUTICAL
INDUSTRY ASSOCIATION,

Defendant-Appellant.

Judgment

ON APPEAL from the UNITED STATES DISTRICT COURT
EASTERN DISTRICT OF VIRGINIA

in CASE NOS. 95-CV-1005, 95-CV-1052, 95-CV-1103, 95-CV-1236

This CAUSE having been heard and considered, it is

ORDERED and ADJUDGED:

AFFIRMED-IN PART,
REVERSED-IN-PART AND REMANDED

ENTERED BY ORDER
OF THE COURT

DATED APR 04 1996

Francis X. Gindhart, Clerk

ISSUED AS A MANDATE: July 19, 1996

APPENDIX N

TITLE 35. PATENTS
PART II. PATENTABILITY OF INVENTIONS
AND GRANT OF PATENTS
CHAPTER 14. ISSUE OF PATENT

35 USC § 154 (Supp. 1996)

§ 154. Contents and term of patent

(a) In general.-

(1) Contents. -- Every patent shall contain a short title of the invention and a grant to the patentee, his heirs or assigns, of the right to exclude others from making, using, offering for sale, or selling the invention throughout the United States or importing the invention into the United States, and, if the invention is a process, of the right to exclude others from using, offering for sale or selling throughout the United States, or importing into the United States, products made by that process, referring to the specification for the particulars thereof.

(2) Term. -- Subject to the payment of fees under this title, such grant shall be for a term beginning on the date on which the patent issues and ending 20 years from the date on which the application for the patent was filed in the United States or, if the application contains a specific reference to an earlier filed application or applications under section 120,

121, or 365(c) of this title, from the date on which the earliest such application was filed.

(3) Priority. -- Priority under section 119, 365(a), or 365(b) of this title shall not be taken into account in determining the term of a patent.

(4) Specification and drawing. -- A copy of the specification and drawing shall be annexed to the patent and be a part of such patent.

(b) Term extension. --

(1) Interference delay or secrecy orders. -- If the issue of an original patent is delayed due to a proceeding under section 135(a) of this title, or because the application for patent is placed under an order pursuant to section 181 of this title, the term of the patent shall be extended for the period of delay, but in no case more than 5 years.

(2) Extension for appellate review. -- If the issue of a patent is delayed due to appellate review by the Board of Patent Appeals and Interferences or by a Federal court and the patent is issued pursuant to a decision in the review reversing an adverse determination of patentability, the term of the patent shall be extended for a period of time but in no case more than 5 years. A patent shall not be eligible for extension under this paragraph if it is subject to a terminal disclaimer due to the issue of another patent

claiming subject matter that is not patentably distinct from that under appellate review.

(3) Limitations. -- The period of extension referred to in paragraph (2)--

(A) shall include any period beginning on the date on which an appeal is filed under section 134 or 141 of this title, or on which an action is commenced under section 145 of this title, and ending on the date of a final decision in favor of the applicant;

(B) shall be reduced by any time attributable to appellate review before the expiration of 3 years from the filing date of the application for patent; and

(C) shall be reduced for the period of time during which the applicant for patent did not act with due diligence, as determined by the Commissioner.

(4) Length of extension. -- The total duration of all extensions of a patent under this subsection shall not exceed 5 years.

(c) Continuation. --

(1) Determination. -- The term of a patent that is in force on or that results from an application filed before the date that is 6 months after the date of the

enactment of the Uruguay Round Agreements Act shall be the greater of the 20-year term as provided in subsection (a), or 17 years from grant, subject to any terminal disclaimers.

(2) Remedies. -- The remedies of sections 283, 284, and 285 of this title shall not apply to Acts which--

(A) were commenced or for which substantial investment was made before the date that is 6 months after the date of the enactment of the Uruguay Round Agreements Act; and

(B) became infringing by reason of paragraph (1).

(3) Remuneration. -- The acts referred to in paragraph (2) may be continued only upon the payment of an equitable remuneration to the patentee that is determined in an action brought under chapter 28 and chapter 29 (other than those provisions excluded by paragraph (2)) of this title.

APPENDIX O

TITLE 35. PATENTS
PART II. PATENTABILITY OF INVENTIONS AND GRANT OF PATENTS
CHAPTER 14. ISSUE OF PATENT

35 USC § 156 (Supp. 1996)

§ 156. Extension of patent term

(a) The term of a patent which claims a product, a method of using a product, or a method of manufacturing a product shall be extended in accordance with this section from the original expiration date of the patent if--

(1) the term of the patent has not expired before an application is submitted under subsection (d)(1) for its extension;

(2) the term of the patent has never been extended under subsection (e)(1) of this section;

(3) an application for extension is submitted by the owner of record of the patent or its agent and in accordance with the requirements of paragraphs (1) through (4) of subsection (d);

(4) the product has been subject to a regulatory review period before its commercial marketing or use;

(5)(A) except as provided in subparagraph (B) or (C), the permission for the commercial marketing or use of the product after such regulatory review period is the first permitted commercial marketing or use of the product under the provision of law under which such regulatory review period occurred;

(B) in the case of a patent which claims a method of manufacturing the product which primarily uses recombinant DNA technology in the manufacture of the product, the permission for the commercial marketing or use of the product after such regulatory review period is the first permitted commercial marketing or use of a product manufactured under the process claimed in the patent; or

(C) for purposes of subparagraph (A), in the case of a patent which--

(i) claims a new animal drug or a veterinary biological product which (I) is not covered by the claims in any other patent which has been extended, and (II) has received permission for the commercial marketing or use in non-food-producing animals and in food-producing animals, and

(ii) was not extended on the basis of the regulatory review period for use in non-food-producing animals, the permission for the commercial marketing or use of the drug or product after the regulatory review period for use

in food-producing animals is the first permitted commercial marketing or use of the drug or product for administration to a food-producing animal.

The product referred to in paragraphs (4) and (5) is hereinafter in this section referred to as the "approved product".

(b) Except as provided in subsection (d)(5)(F), the rights derived from any patent the term of which is extended under this section shall during the period during which the term of the patent is extended--

(1) in the case of a patent which claims a product, be limited to any use approved for the product--

(A) before the expiration of the term of the patent--

(i) under the provision of law under which the applicable regulatory review occurred, or

(ii) under the provision of law under which any regulatory review described in paragraph (1), (4), or (5) of subsection (g) occurred, and

(B) on or after the expiration of the regulatory review period upon which the extension of the patent was based;

(2) in the case of a patent which claims a method of using a product, be limited to any use claimed by the patent and approved for the product--

(A) before the expiration of the term of the patent--

(i) under any provision of law under which an applicable regulatory review occurred, and

(ii) under the provision of law under which any regulatory review described in paragraph (1), (4), or (5) of subsection (g) occurred, and

(B) on or after the expiration of the regulatory review period upon which the extension of the patent was based; and

(3) in the case of a patent which claims a method of manufacturing a product, be limited to the method of manufacturing as used to make--

(A) the approved product, or

(B) the product if it has been subject to a regulatory review period described in paragraphs (1), (4), or (5) of subsection (g).

As used in this subsection, the term "product" includes an approved product.

(c) The term of a patent eligible for extension under subsection (a) shall be extended by the time equal to the regulatory review period for the approved product which period occurs after the date the patent is issued, except that--

(1) each period of the regulatory review period shall be reduced by any period determined under subsection (d)(2)(B) during which the applicant for the patent extension did not act with due diligence during such period of the regulatory review period;

(2) after any reduction required by paragraph (1), the period of extension shall include only one-half of the time remaining in the periods described in paragraphs (1)(B)(i), (2)(B)(i), (3)(B)(i), (4)(B)(i), and (5)(B)(i) of subsection (g);

(3) if the period remaining in the term of a patent after the date of the approval of the approved product under the provision of law under which such regulatory review occurred when added to the regulatory review period as revised under paragraphs (1) and (2) exceeds fourteen years, the period of extension shall be reduced so that the total of both such periods does not exceed fourteen years; and

(4) in no event shall more than one patent be extended under subsection (e)(1) for the same regulatory review period for any product.

(d)(1) To obtain an extension of the term of a patent under this section, the owner of record of the patent or its agent shall submit an application to the Commissioner. Except as provided in paragraph (5), such an application may only be submitted within the sixty-day period beginning on the date the product received permission under the provision of law under which the applicable regulatory review period occurred for commercial marketing or use. The application shall contain--

(A) the identity of the approved product and the Federal statute under which regulatory review occurred;

(B) the identity of the patent for which an extension is being sought and the identity of each claim of such patent which claims the approved product or a method of using or manufacturing the approved product;

(C) information to enable the Commissioner to determine under subsections (a) and (b) the eligibility of a patent for extension and the rights that will be derived from the extension and information to enable the Commissioner and the Secretary of Health and Human Services or the Secretary of Agriculture to determine the period of the extension under subsection (g);

(D) a brief description of the activities undertaken by the applicant during the applicable regulatory review period with respect to the approved product and the significant dates applicable to such activities; and

(E) such patent or other information as the Commissioner may require.

(2)(A) Within 60 days of the submittal of an application for extension of the term of a patent under paragraph (1), the Commissioner shall notify--

(i) the Secretary of Agriculture if the patent claims a drug product or a method of using or manufacturing a drug product and the drug product is subject to the Virus-Serum-Toxin Act, and

(ii) the Secretary of Health and Human Services if the patent claims any other drug product, a medical device, or a food additive or color additive or a method of using or manufacturing such a product, device, or additive and if the product, device, and additive are subject to the Federal Food, Drug, and Cosmetic Act, of the extension application and shall submit to the Secretary who is so notified a copy of the application. Not later than 30 days after the receipt of an application from the Commissioner, the Secretary receiving the application shall review the dates contained in the application pursuant to paragraph (1)(C) and determine the applicable regulatory review period, shall notify the Commissioner of the determination, and shall publish in the Federal Register a notice of such determination.

(B)(i) If a petition is submitted to the Secretary making the determination under subparagraph (A), not later than 180 days after the publication of the determination under

subparagraph (A), upon which it may reasonably be determined that the applicant did not act with due diligence during the applicable regulatory review period, the Secretary making the determination shall, in accordance with regulations promulgated by such Secretary, determine if the applicant acted with due diligence during the applicable regulatory review period. The Secretary making the determination shall make such determination not later than 90 days after the receipt of such a petition. For a drug product, device, or additive subject to the Federal Food, Drug, and Cosmetic Act or the Public Health Service Act, the Secretary may not delegate the authority to make the determination prescribed by this clause to an office below the Office of the Commissioner of Food and Drugs. For a product subject to the Virus-Serum-Toxin Act, the Secretary of Agriculture may not delegate the authority to make the determination prescribed by this clause to an office below the office of the
Assistant Secretary for Marketing and Inspection Services.

(ii) The Secretary making a determination under clause (i) shall notify the Commissioner of the determination and shall publish in the Federal Register a notice of such determination together with the factual and legal basis for such determination. Any interested person may request, within the 60-day period beginning on the publication of a determination, the Secretary making the determination to hold an informal hearing on the determination. If such a request is made within such period, such Secretary shall hold such hearing not later than 30 days after the date of the request, or at the request of the person making the request, not later than 60 days after such date. The

Secretary who is holding the hearing shall provide notice of the hearing to the owner of the patent involved and to any interested person and provide the owner and any interested person an opportunity to participate in the hearing. Within 30 days after the completion of the hearing, such Secretary shall affirm or revise the determination which was the subject of the hearing and shall notify the Commissioner of any revision of the determination and shall publish any such revision in the Federal Register.

(3) For the purposes of paragraph (2)(B), the term "due diligence" means that degree of attention, continuous directed effort, and timeliness as may reasonably be expected from, and are ordinarily exercised by, a person during a regulatory review period.

(4) An application for the extension of the term of a patent is subject to the disclosure requirements prescribed by the Commissioner.

(5)(A) If the owner of record of the patent or its agent reasonably expects that the applicable regulatory review period described in paragraph (1)(B)(ii), (2)(B)(ii), (3)(B)(ii), (4)(B)(ii), or (5)(B)(ii) of subsection (g) that began for a product that is the subject of such patent may extend beyond the expiration of the patent term in effect, the owner or its agent may submit an application to the Commissioner for an interim extension during the period beginning 6 months, and ending 15 days, before such term is due to expire. The application shall contain--

(i) the identity of the product subject to regulatory review and the Federal statute under which such review is occurring;

(ii) the identity of the patent for which interim extension is being sought and the identity of each claim of such patent which claims the product under regulatory review or a method of using or manufacturing the product;

(iii) information to enable the Commissioner to determine under subsection (a)(1), (2), and (3) the eligibility of a patent for extension;

(iv) a brief description of the activities undertaken by the applicant during the applicable regulatory review period to date with respect to the product under review and the significant dates applicable to such activities; and

(v) such patent or other information as the Commissioner may require.

(B) If the Commissioner determines that, except for permission to market or use the product commercially, the patent would be eligible for an extension of the patent term under this section, the Commissioner shall publish in the Federal Register a notice of such determination, including the identity of the product under regulatory review, and shall issue to the applicant a certificate of interim extension for a period of not more than 1 year.

(C) The owner of record of a patent, or its agent, for which an interim extension has been granted under subparagraph (B), may apply for not more than 4 subsequent interim extensions under this paragraph, except that, in the case of a patent subject to subsection (g)(6)(C), the owner of record of the patent, or its agent, may apply for only 1 subsequent interim extension under this paragraph. Each such subsequent application shall be made during the period beginning 60 days before, and ending 30 days before, the expiration of the preceding interim extension.

(D) Each certificate of interim extension under this paragraph shall be recorded in the official file of the patent and shall be considered part of the original patent.

(E) Any interim extension granted under this paragraph shall terminate at the end of the 60-day period beginning on the date on which the product involved receives permission for commercial marketing or use, except that, if within that 60-day period the applicant notifies the Commissioner of such permission and submits any additional information under paragraph (1) of this subsection not previously contained in the application for interim extension, the patent shall be further extended, in accordance with the provisions of this section--

(i) for not to exceed 5 years from the date of expiration of the original patent term; or

(ii) if the patent is subject to subsection (g)(6)(C), from the date on which the product involved receives approval for commercial marketing or use.

(F) The rights derived from any patent the term of which is extended under this paragraph shall, during the period of interim extension--

(i) in the case of a patent which claims a product, be limited to any use then under regulatory review;

(ii) in the case of a patent which claims a method of using a product, be limited to any use claimed by the patent then under regulatory review; and

(iii) in the case of a patent which claims a method of manufacturing a product, be limited to the method of manufacturing as used to make the product then under regulatory review.

(e)(1) A determination that a patent is eligible for extension may be made by the Commissioner solely on the basis of the representations contained in the application for the extension. If the Commissioner determines that a patent is eligible for extension under subsection (a) and that the requirements of paragraphs (1) through (4) of subsection (d) have been complied with, the Commissioner shall issue to the applicant for the extension of the term of the patent a certificate of extension, under seal, for the period prescribed by subsection (c). Such certificate shall be recorded in the official file of the patent and shall be considered as part of the original patent.

(2) If the term of a patent for which an application has been submitted under subsection (d)(1) would expire before a certificate of extension is issued or denied under paragraph (1) respecting the application, the Commissioner shall extend, until such determination is made, the term of the patent for periods of up to one year if he determines that the patent is eligible for extension.

(f) For purposes of this section:

(1) The term "product" means:

(A) A drug product.

(B) Any medical device, food additive, or color additive subject to regulation under the Federal Food, Drug, and Cosmetic Act.

(2) The term "drug product" means the active ingredient of--

(A) a new drug, antibiotic drug, or human biological product (as those terms are used in the Federal Food, Drug, and Cosmetic Act and the Public Health Service Act), or

(B) a new animal drug or veterinary biological product (as those terms are used in the Federal Food, Drug, and Cosmetic Act and the Virus-Serum-Toxin Act) which is not primarily manufactured using recombinant DNA, recombinant RNA, hybridoma technology, or other

processes involving site specific genetic manipulation techniques, including any salt or ester of the active ingredient, as a single entity or in combination with another active ingredient.

(3) The term "major health or environmental effects test" means a test which is reasonably related to the evaluation of the health or environmental effects of a product, which requires at least six months to conduct, and the data from which is submitted to receive permission for commercial marketing or use. Periods of analysis or evaluation of test results are not to be included in determining if the conduct of a test required at least six months.

(4)(A) Any reference to section 351 is a reference to section 351 of the Public Health Service Act.

(B) Any reference to section 503, 505, 507, 512, or 515 is a reference to section 503, 505, 507, 512, or 515 of the Federal Food, Drug, and Cosmetic Act.

(C) Any reference to the Virus-Serum-Toxin Act is a reference to the Act of March 4, 1913 (21 U.S.C. 151-158).

(5) The term "informal hearing" has the meaning prescribed for such term by section 201(y) of the Federal Food, Drug, and Cosmetic Act.

(6) The term "patent" means a patent issued by the United States Patent and Trademark Office.

(7) The term "date of enactment" as used in this section means September 24, 1984, for a human drug product, a medical device, food additive, or color additive.

(8) The term "date of enactment" as used in this section means the date of enactment of the Generic Animal Drug and Patent Term Restoration Act for an animal drug or a veterinary biological product.

(g) For purposes of this section, the term "regulatory review period" has the following meanings:

(1)(A) In the case of a product which is a new drug, antibiotic drug, or human biological product, the term means the period described in subparagraph (B) to which the limitation described in paragraph (6) applies.

(B) The regulatory review period for a new drug, antibiotic drug, or human biological product is the sum of--

(i) the period beginning on the date an exemption under subsection (i) of section 505 or subsection (d) of section 507 became effective for the approved product and ending on the date an application was initially submitted for such drug product under section 351, 505, or 507, and

(ii) the period beginning on the date the application was initially submitted for the approved

product under section 351, subsection (b) of section 505, or section 507 and ending on the date such application was approved under such section.

(2)(A) In the case of a product which is a food additive or color additive, the term means the period described in subparagraph (B) to which the limitation described in paragraph (6) applies.

(B) The regulatory review period for a food or color additive is the sum of--

(i) the period beginning on the date a major health or environmental effects test on the additive was initiated and ending on the date a petition was initially submitted with respect to the product under the Federal Food, Drug, and Cosmetic Act requesting the issuance of a regulation for use of the product, and

(ii) the period beginning on the date a petition was initially submitted with respect to the product under the Federal Food, Drug, and Cosmetic Act requesting the issuance of a regulation for use of the product, and ending on the date such regulation became effective or, if objections were filed to such regulation, ending on the date such objections were resolved and commercial marketing was permitted or, if commercial marketing was permitted and later revoked pending further proceedings as a result of such objections, ending

on the date such proceedings were finally resolved and commercial marketing was permitted.

(3)(A) In the case of a product which is a medical device, the term means the period described in subparagraph (B) to which the limitation described in paragraph (6) applies.

(B) The regulatory review period for a medical device is the sum of--

(i) the period beginning on the date a clinical investigation on humans involving the device was begun and ending on the date an application was initially submitted with respect to the device under section 515, and

(ii) the period beginning on the date an application was initially submitted with respect to the device under section 515 and ending on the date such application was approved under such Act or the period beginning on the date a notice of completion of a product development protocol was initially submitted under section 515(f)(5) and ending on the date the protocol was declared completed under section 515(f)(6).

(4)(A) In the case of a product which is a new animal drug, the term means the period described in subparagraph (B) to which the limitation described in paragraph (6) applies.

(B) The regulatory review period for a new animal drug product is the sum of--

(i) the period beginning on the earlier of the date a major health or environmental effects test on the drug was initiated or the date an exemption under subsection (j) of section 512 became effective for the approved new animal drug product and ending on the date an application was initially submitted for such animal drug product under section 512, and

(ii) the period beginning on the date the application was initially submitted for the approved animal drug product under subsection (b) of section 512 and ending on the date such application was approved under such section.

(5)(A) In the case of a product which is a veterinary biological product, the term means the period described in subparagraph (B) to which the limitation described in paragraph (6) applies.

(B) The regulatory period for a veterinary biological product is the sum of--

(i) the period beginning on the date the authority to prepare an experimental biological product under the Virus-Serum-Toxin Act became effective and ending on the date an application for a license was submitted under the Virus-Serum-Toxin Act, and

(ii) the period beginning on the date an application for a license was initially submitted for approval under the Virus-Serum-Toxin Act and ending on the date such license was issued.

(6) A period determined under any of the preceding paragraphs is subject to the following limitations:

(A) If the patent involved was issued after the date of the enactment of this section, the period of extension determined on the basis of the regulatory review period determined under any such paragraph may not exceed five years.

(B) If the patent involved was issued before the date of the enactment of this section and--

(i) no request for an exemption described in paragraph (1)(B) or (4)(B) was submitted and no request for the authority described in paragraph (5)(B) was submitted,

(ii) no major health or environmental effects test described in paragraph (2)(B) or (4)(B) was initiated and no petition for a regulation or application for registration described in such paragraph was submitted, or

(iii) no clinical investigation described in paragraph (3) was begun or product development protocol described in such paragraph was submitted, before such date for

the approved product the period of extension determined on the basis of the regulatory review period determined under any such paragraph may not exceed five years.

(C) If the patent involved was issued before the date of the enactment of this section and if an action described in subparagraph (B) was taken before the date of the enactment of this section with respect to the approved product and the commercial marketing or use of the product has not been approved before such date, the period of extension determined on the basis of the regulatory review period determined under such paragraph may not exceed two years or in the case of an approved product which is a new animal drug or veterinary biological product (as those terms are used in the Federal Food, Drug, and Cosmetic Act or the Virus-Serum-Toxin Act), three years.

(h) The Commissioner may establish such fees as the Commissioner determines appropriate to cover the costs to the Office of receiving and acting upon applications under this section.

APPENDIX P

TITLE 5. GOVERNMENT ORGANIZATION
AND EMPLOYEES
PART I. THE AGENCIES
CHAPTER 5. ADMINISTRATIVE PROCEDURE

5 USC § 553 (1996)

§ 553. Rule making

(a) This section applies, according to the provisions thereof, except to the extent that there is involved--

(1) a military or foreign affairs function of the United States; or

(2) a matter relating to agency management or personnel or to public property, loans, grants, benefits, or contracts.

(b) General notice of proposed rule making shall be published in the Federal Register, unless persons subject thereto are named and either personally served or otherwise have actual notice thereof in accordance with law. The notice shall include--

(1) a statement of the time, place, and nature of public rule making proceedings;

(2) reference to the legal authority under which the rule is proposed; and

(3) either the terms or substance of the proposed rule or a description of the subjects and issues involved.

Except when notice or hearing is required by statute, this subsection does not apply--

(A) to interpretative rules, general statements of policy, or rules of agency organization, procedure, or practice; or

(B) when the agency for good cause finds (and incorporates the finding and a brief statement of reasons therefor in the rules issued) that notice and public procedure thereon are impracticable, unnecessary, or contrary to the public interest.

(c) After notice required by this section, the agency shall give interested persons an opportunity to participate in the rule making through submission of written data, views, or arguments with or without opportunity for oral presentation. After consideration of the relevant matter presented, the agency shall incorporate in the rules adopted a concise general statement of their basis and purpose. When rules are required by statute to be made on the record after opportunity for an agency hearing, sections 556 and 557 of this title apply instead of this subsection.

(d) The required publication or service of a substantive rule shall be made not less than 30 days before its effective date, except--

(1) a substantive rule which grants or recognizes an exemption or relieves a restriction;

(2) interpretative rules and statements of policy; or

(3) as otherwise provided by the agency for good cause found and published with the rule.

(e) Each agency shall give an interested person the right to petition for the issuance, amendment, or repeal of a rule.

APPENDIX Q

TITLE 21. FOOD AND DRUGS
CHAPTER 9. FEDERAL FOOD, DRUG, AND COSMETIC ACT
DRUGS AND DEVICES

21 USC § 355 (Supp. 1996)

§ 355. New drugs

(a) Necessity of effective approval of application

No person shall introduce or deliver for introduction into interstate commerce any new drug, unless an approval of an application filed pursuant to subsection (b) or (j) is effective with respect to such drug.

(b) Filing application; contents

(1) Any person may file with the Secretary an application with respect to any drug subject to the provisions of subsection (a) of this section. Such person shall submit to the Secretary as a part of the application (A) full reports of investigations which have been made to show whether or not such drug is safe for use and whether such drug is effective in use; (B) a full list of the articles used as components of such drug; (C) a full statement of the composition of such drug; (D) a full description of the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such drug; (E) such samples of such drug and of the articles used as

components thereof as the Secretary may require; and (F) specimens of the labeling proposed to be used for such drug. The applicant shall file with the application the patent number and the expiration date of any patent which claims the drug for which the applicant submitted the application or which claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug. If an application is filed under this subsection for a drug and a patent which claims such drug or a method of using such drug is issued after the filing date but before approval of the application, the applicant shall amend the application to include the information required by the preceding sentence. Upon approval of the application, the Secretary shall publish information submitted under the two preceding sentences.

(2) An application submitted under paragraph (1) for a drug for which the investigations described in clause (A) of such paragraph and relied upon by the applicant for approval of the application were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted shall also include--

(A) a certification, in the opinion of the applicant and to the best of his knowledge, with respect to each patent which claims the drug for which such investigations were conducted or which claims a use for such drug for which the applicant is seeking approval under this subsection and for which information is required to be

filed under paragraph (1) or subsection (c) of this section --

(i) that such patent information has not been filed,

(ii) that such patent has expired,

(iii) of the date on which such patent will expire, or

(iv) that such patent is invalid or will not be infringed by the manufacture, use, or sale of the new drug for which the application is submitted; and

(B) if with respect to the drug for which investigations described in paragraph (1)(A) were conducted information was filed under paragraph (1) or subsection (c) of this section for a method of use patent which does not claim a use for which the applicant is seeking approval under this subsection, a statement that the method of use patent does not claim such a use.

(3)(A) An applicant who makes a certification described in paragraph (2)(A)(iv) shall include in the application a statement that the applicant will give the notice required by subparagraph (B) to--

(i) each owner of the patent which is the subject of the certification or the representative of such owner designated to receive such notice, and

(ii) the holder of the approved application under subsection (b) of this section for the drug which is

claimed by the patent or a use of which is claimed by the patent or the representative of such holder designated to receive such notice.

(B) The notice referred to in subparagraph (A) shall state that an application has been submitted under this subsection for the drug with respect to which the certification is made to obtain approval to engage in the commercial manufacture, use, or sale of the drug before the expiration of the patent referred to in the certification. Such notice shall include a detailed statement of the factual and legal basis of the applicant's opinion that the patent is not valid or will not be infringed.

(C) If an application is amended to include a certification described in paragraph (2)(A)(iv), the notice required by subparagraph (B) shall be given when the amended application is submitted.

(c) Period for approval of application; period for, notice, and expedition of hearing; period for issuance of order

(1) Within one hundred and eighty days after the filing of an application under subsection (b), or such additional period as may be agreed upon by the Secretary and the applicant, the Secretary shall either--

(A) Approve the application if he then finds that none of the grounds for denying approval specified in subsection (d) of this section applies, or

(B) Give the applicant notice of an opportunity for a hearing before the Secretary under subsection (d) of this section on the question whether such application is approvable. If the applicant elects to accept the opportunity for hearing by written request within thirty days after such notice, such hearing shall commence not more than ninety days after the expiration of such thirty days unless the Secretary and the applicant otherwise agree. Any such hearing shall thereafter be conducted on an expedited basis and the Secretary's order thereon shall be issued within ninety days after the date fixed by the Secretary for filing final briefs.

(2) If the patent information described in subsection (b) of this section could not be filed with the submission of an application under subsection (b) of this section because the application was filed before the patent information was required under subsection (b) of this section or a patent was issued after the application was approved under such subsection, the holder of an approved application shall file with the Secretary the patent number and the expiration date of any patent which claims the drug for which the application was submitted or which claims a method of using such drug and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use, or sale of the drug. If the holder of an approved application could not file patent information under subsection (b) of this section because it was not required at the time the application was approved, the holder shall file such information under this subsection not later than thirty days after September 24, 1984 and if the

holder of an approved application could not file patent information under subsection (b) of this section because no patent had been issued when an application was filed or approved, the holder shall file such information under this subsection not later than thirty days after the date the patent involved is issued. Upon the submission of patent information under this subsection, the Secretary shall publish it.

(3) The approval of an application filed under subsection (b) of this section which contains a certification required by paragraph (2) of such subsection shall be made effective on the last applicable date determined under the following:

(A) If the applicant only made a certification described in clause (i) or (ii) of subsection (b)(2)(A) or in both such clauses, the approval may be made effective immediately.

(B) If the applicant made a certification described in clause (iii) of subsection (b)(2)(A) of this section, the approval may be made effective on the date certified under clause (iii).

(C) If the applicant made a certification described in clause (iv) of subsection (b)(2)(A) of this section, the approval shall be made effective immediately unless an action is brought for infringement of a patent which is the subject of the certification before the expiration of forty-five days from the date the notice provided under paragraph (3)(B) is received. If such an action is

brought before the expiration of such days, the approval may be made effective upon the expiration of the thirty-month period beginning on the date of the receipt of the notice provided under paragraph (3)(B) or such shorter or longer period as the court may order because either party to the action failed to reasonably cooperate in expediting the action, except that--

(i) if before the expiration of such period the court decides that such patent is invalid or not infringed, the approval may be made effective on the date of the court decision.

(ii) If before the expiration of such period the court decides that such patent has been infringed, the approval may be made effective on such date as the court orders under section 271(e)(4)(A) of Title 35, United States Code, or

(iii) if before the expiration of such period the court grants a preliminary injunction prohibiting the applicant from engaging in the commercial manufacture or sale of the drug until the court decides the issues of patent validity and infringement and if the court decides that such patent is invalid or not infringed, the approval shall be made effective on the date of such court decision.

In such an action, each of the parties shall reasonably cooperate in expediting the action. Until the expiration of forty-five days from the date the notice made under paragraph (3)(B) is received, no action may be brought

under section 2201, shall be brought in the judicial district where the defendant has its principal place of business or a regular and established place of business.

(D)(i) If an application (other than an abbreviated new drug application) submitted under subsection (b) of this section for a drug, no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application under subsection (b), was approved during the period beginning January 1, 1982, and ending on September 24, 1984, the Secretary may not make the approval of another application for a drug for which the investigations described in clause (A) of subsection (b)(1) of this section and relied upon by the applicant for approval of the application were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted effective before the expiration of ten years from the date of the approval of the application previously approved under subsection (b) of this section.

(ii) If an application submitted under subsection (b) for a drug, no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application under subsection (b) of this section, is approved after September 24, 1984, no application which refers to the drug for which the subsection (b) application was submitted and for which the investigations described in clause (A) of subsection (b)(1) of this section and relied upon by the applicant for approval of the application were not conducted by or

for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted may be submitted under subsection (b) of this section before the expiration of five years from the date of the approval of the application under subsection (b) of this section, except that such an application may be submitted under subsection (b) of this section after the expiration of four years from the date of the approval of the subsection (b) application if it contains a certification of patent invalidity or noninfringement described in clause (iv) of subsection (b)(2)(A) of this section. The approval of such an application shall be made effective in accordance with this paragraph except that, if an action for patent infringement is commenced during the one-year period beginning forty-eight months after the date of the approval of the subsection (b) application, the thirty-month period referred to in subparagraph (C) shall be extended by such amount of time (if any) which is required for seven and one-half years to have elapsed from the date of approval of the subsection (b) application.

(iii) If an application submitted under subsection (b) of this section for a drug, which includes an active ingredient (including any ester or salt of the active ingredient) that has been approved in another application approved under subsection (b) of this section, is approved after September 24, 1984, and if such application contains reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and

conducted or sponsored by the applicant, the Secretary may not make the approval of an application submitted under subsection (b) of this section for the conditions of approval of such drug in the approved subsection (b) application effective before the expiration of three years from the date of the approval of the application under subsection (b) of this section if the investigations described in clause (A) of subsection (b)(1) of this section and relied upon by the applicant for approval of the application were not conducted by or for the applicant and if the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted.

(iv) If a supplement to an application approved under subsection (b) of this section is approved after September 24, 1984, and the supplement contains reports of new clinical investigation (other than bioavailability studies) essential to the approval of the supplement and conducted or sponsored by the person submitting the supplement, the Secretary may not make the approval of an application submitted under subsection (b) of this section for a change approved in the supplement effective before the expiration of three years from the date of the approval of the supplement under subsection (b) if the investigations described in clause (A) of subsection (b)(1) of this section and relied upon by the applicant for approval of the application were not conducted by or for the applicant and if the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted.

(v) If an application (or supplement to an application) submitted under subsection (b) for a drug, which includes an active ingredient (including any ester or salt of the active ingredient) that has been approved in another application under subsection (b) of this section, was approved during the period beginning January 1, 1982, and ending on September 24, 1984, the Secretary may not make the approval of an application submitted under this subsection and for which the investigations described in clause (A) of subsection (b)(1) of this section and relied upon by the applicant for approval of the application were not conducted by or for the applicant and for which the applicant has not obtained a right of reference or use from the person by or for whom the investigations were conducted and which refers to the drug for which the subsection (b) application was submitted effective before the expiration of two years from September 24, 1984.

(d) Grounds for refusing application; approval of application; "substantial evidence" defined

If the Secretary finds, after due notice to the applicant in accordance with subsection (c) of this section and giving him an opportunity for a hearing, in accordance with said subsection, that (1) the investigations, reports of which are required to be submitted to the Secretary pursuant to subsection (b) of this section, do not include adequate tests by all methods reasonably applicable to show whether or not such drug is safe for use under the conditions prescribed, recommended, or suggested in the proposed labeling thereof; (2) the results of such tests show that

such drug is unsafe for use under such conditions or do not show that such drug is safe for use under such conditions; (3) the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such drug are inadequate to preserve its identity, strength, quality, and purity; (4) upon the basis of the information submitted to him as part of the application, or upon the basis of any other information before him with respect to such drug, he has insufficient information to determine whether such drug is safe for use under such conditions; or (5) evaluated on the basis of the information submitted to him as part of the application and any other information before him with respect to such drug, there is a lack of substantial evidence that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the proposed labeling thereof; or (6) the application failed to contain the patent information prescribed by subsection (b) of this section ; or (7) based on a fair evaluation of all material facts, such labeling is false or misleading in any particular; he shall issue an order refusing to approve the application. If, after such notice and opportunity for hearing, the Secretary finds that clauses (1) through (6) [(7)] do not apply, he shall issue an order approving the application. As used in this subsection and subsection (e) of this section, the term "substantial evidence" means evidence consisting of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved, on the basis of which it could fairly and responsibly be concluded by such experts that the drug

will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling or proposed labeling thereof.

(e) Withdrawal of approval; grounds; immediate suspension upon finding imminent hazard to public health

The Secretary shall, after due notice and opportunity for hearing to the applicant, withdraw approval of an application with respect to any drug under this section if the Secretary finds (1) that clinical or other experience, tests, or other scientific data show that such drug is unsafe for use under the conditions of use upon the basis of which the application was approved; (2) that new evidence of clinical experience, not contained in such application or not available to the Secretary until after such application was approved, or tests by new methods, or tests by methods not deemed reasonably applicable when such application was approved, evaluated together with the evidence available to the Secretary when the application was approved, shows that such drug is not shown to be safe for use under the conditions of use upon the basis of which the application was approved; or (3) on the basis of new information before him with respect to such drug, evaluated together with the evidence available to him when the application was approved, that there is a lack of substantial evidence that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling thereof; or (4) the patent information prescribed by subsection (c) was not filed within thirty days after the receipt of written notice

from the Secretary specifying the failure to file such information; or (5) that the application contains any untrue statement of a material fact: *Provided,* That if the Secretary (or in his absence the officer acting as Secretary) finds that there is an imminent hazard to the public health, he may suspend the approval of such application immediately, and give the applicant prompt notice of his action and afford the applicant the opportunity for an expedited hearing under this subsection; but the authority conferred by this proviso to suspend the approval of an application shall not be delegated. The Secretary may also, after due notice and opportunity for hearing to the applicant, withdraw the approval of an application submitted under subsection (b) or (j) of this section with respect to any drug under this section if the Secretary finds (1) that the applicant has failed to establish a system for maintaining required records, or has repeatedly or deliberately failed to maintain such records or to make required reports, in accordance with a regulation or order under subsection (k) of this section or to comply with the notice requirements of section 360(k)(2) of this title, or the applicant has refused to permit access to, or copying or verification of, such records as required by paragraph (2) of such subsection; or (2) that on the basis of new information before him, evaluated together with the evidence before him when the application was approved, the methods used in, or the facilities and controls used for, the manufacture, processing, and packing of such drug are inadequate to assure and preserve its identity, strength, quality, and purity and were not made adequate within a reasonable time after receipt of written notice from the Secretary specifying the matter complained of; or (3) that on the

basis of new information before him, evaluated together with the evidence before him when the application was approved, the labeling of such drug, based on a fair evaluation of all material facts, is false or misleading in any particular and was not corrected within a reasonable time after receipt of written notice from the Secretary specifying the matter complained of. Any order under this subsection shall state the findings upon which it is based.

Revocation of order refusing, withdrawing or suspending approval of application

(f) Whenever the Secretary finds that the facts so require, he shall revoke any previous order under subsection (d) or (e) of this section refusing, withdrawing, or suspending approval of an application and shall approve such application or reinstate such approval, as may be appropriate.

Service of Orders

(g) Orders of the Secretary issued under this section shall be served (1) in person by any officer or employee of the Department designated by the Secretary or (2) by mailing the order by registered mail or by certified mail addressed to the applicant or respondent at his last known address in the records of the Secretary.

Appeal from order

(h) An appeal may be taken by the applicant from an order of the Secretary refusing or withdrawing approval of

an application under this section. Such appeal shall be taken by filing in the United States court of appeals for the circuit wherein such applicant resides or has his principal place of business, or in the United States Court of Appeals for the District of Columbia Circuit, within sixty days after the entry of such order, a written petition praying that the order of the Secretary be set aside. A copy of such petition shall be forthwith transmitted by the clerk of the court to the Secretary, or any officer designated by him for that purpose, and thereupon the Secretary shall certify and file in the court the record upon which the order complained of was entered, as provided in section 2112 of Title 28. Upon the filing of such petition such court shall have exclusive jurisdiction to affirm or set aside such order, except that until the filing of the record the Secretary may modify or set aside his order. No objection to the order of the Secretary shall be considered by the court unless such objection shall have been urged before the Secretary or unless there were reasonable grounds for failure so to do. The finding of the Secretary as to the facts, if supported by substantial evidence, shall be conclusive. If any person shall apply to the court for leave to adduce additional evidence, and shall show to the satisfaction of the court that such additional evidence is material and that there were reasonable grounds for failure to adduce such evidence in the proceeding before the Secretary, the court may order such additional evidence to be taken before the Secretary and to be adduced upon the hearing in such manner and upon such terms and conditions as to the court may seem proper. The Secretary may modify his findings as to the facts by reason of the additional evidence so taken, and he shall file with the court such modified

findings which, if supported by substantial evidence, shall be conclusive, and his recommendation, if any, for the setting aside of the original order. The judgment of the court affirming or setting aside any such order of the Secretary shall be final, subject to review by the Supreme Court of the United States upon certiorari or certification as provided in section 1254 of Title 28. The commencement of proceedings under this subsection shall not, unless specifically ordered by the court to the contrary, operate as a stay
of the Secretary's order.

Exemptions of drugs for research; discretionary and mandatory conditions; direct reports to Secretary

(i) The Secretary shall promulgate regulations for exempting from the operation of the foregoing subsections of this section drugs intended solely for investigational use by experts qualified by scientific training and experience to investigate the safety and effectiveness of drugs. Such regulations may, within the discretion of the Secretary, among other conditions relating to the protection of the public health, provide for conditioning such exemption upon--

(1) the submission to the Secretary, before any clinical testing of a new drug is undertaken, of reports, by the manufacturer or the sponsor of the investigation of such drug, of preclinical tests (including tests on animals) of such drug adequate to justify the proposed clinical testing;

(2) the manufacturer or the sponsor of the investigation of a new drug proposed to be distributed to investigators for clinical testing obtaining a signed agreement from each of such investigators that patients to whom the drug is administered will be under his personal supervision, or under the supervision of investigators responsible to him, and that he will not supply such drug to any other investigator, or to clinics, for administration to human beings; and

(3) the establishment and maintenance of such records, and the making of such reports to the Secretary, by the manufacturer or the sponsor of the investigation of such drug, of data (including but not limited to analytical reports by investigators) obtained as the result of such investigational use of such drug, as the Secretary finds will enable him to evaluate the safety and effectiveness of such drug in the event of the filing of an application pursuant to subsection (b) of this section.

Such regulations shall provide that such exemption shall be conditioned upon the manufacturer, or the sponsor of the investigation, requiring that experts using such drugs for investigational purposes certify to such manufacturer or sponsor that they will inform any human beings to whom such drugs, or any controls used in connection therewith, are being administered, or their representatives, that such drugs are being used for investigational purposes and will obtain the consent of such human beings or their representatives, except where they deem it not feasible or, in their professional judgment, contrary to the best interests of such human beings. Nothing in this subsection shall be

construed to require any clinical investigator to submit directly to the Secretary reports on the investigational use of drugs.

(j) Abbreviated new drug applications

(1) Any person may file with the Secretary an abbreviated application for the approval of a new drug.

(2)(A) An abbreviated application for a new drug shall contain--

(i) information to show that the conditions of use prescribed, recommended, or suggested in the labeling proposed for the new drug have been previously approved for a drug listed under paragraph (6) (hereinafter in this subsection referred to as a "listed drug");

(ii)(I) if the listed drug referred to in clause (i) has only one active ingredient, information to show that the active ingredient of the new drug is the same as that of the listed drug;

(II) if the listed drug referred to in clause (i) has more than one active ingredient, information to show that the active ingredients of the new drug are the same as those of the listed drug, or

(III) if the listed drug referred to in clause (i) has more than one active ingredient and if one of the active ingredients of the new drug is different and the

application is filed pursuant to the approval of a petition filed under subparagraph (C), information to show that the other active ingredients of the new drug are the same as the active ingredients of the listed drug, information to show that the different active ingredient is an active ingredient of a listed drug or of a drug which does not meet the requirements of section 321(p) of this title, and such other information respecting the different active ingredient with respect to which the petition was filed as the Secretary may require;

(iii) information to show that the route of administration, the dosage form, and the strength of the new drug are the same as those of the listed drug referred to in clause (i) or, if the route of administration, the dosage form, or the strength of the new drug is different and the application is filed pursuant to the approval of a petition filed under subparagraph (C), such information respecting the route of administration, dosage form, or strength with respect to which the petition was filed as the Secretary may require;

(iv) information to show that the new drug is bioequivalent to the listed drug referred to in clause (i), except that if the application is filed pursuant to the approval of a petition filed under subparagraph (C), information to show that the active ingredients of the new drug are of the same pharmacological or therapeutic class as those of the listed drug referred to in clause (i) and the new drug can be expected to have the same therapeutic effect as the listed drug when

administered to patients for a condition of use referred to in clause (i);

(v) information to show that the labeling proposed for the new drug is the same as the labeling approved for the listed drug referred to in clause (i) except for changes required because of differences approved under a petition filed under subparagraph (C) or because the new drug and the listed drug are produced or distributed by different manufacturers;

(vi) the items specified in clauses (B) through (F) of subsection (b)(1) of this section;

(vii) a certification, in the opinion of the applicant and to the best of his knowledge, with respect to each patent which claims the listed drug referred to in clause (i) or which claims a use for such listed drug for which the applicant is seeking approval under this subsection and for which information is required to be filed under subsection (b) or (c)--

(I) that such patent information has not been filed,

(II) that such patent has expired,

(III) of the date on which such patent will expire, or

(IV) that such patent is invalid or will not be infringed by the manufacture, use, or sale of the new drug for which the application is submitted; and

(viii) if with respect to the listed drug referred to in clause (i) information was filed under subsection (b) or (c) of this section for a method of use patent which does not claim a use for which the applicant is seeking approval under this subsection, a statement that the method of use patent does not claim such a use.

The Secretary may not require that an abbreviated application contain information in addition to that required by clauses (i) through (viii).

(B)(i) An applicant who makes a certification described in subparagraph (A)(vii)(IV) shall include in the application a statement that the applicant will give the notice required by clause (ii) to--

(I) each owner of the patent which is the subject of the certification or the representative of such owner designated to receive such notice, and

(II) the holder of the approved application under subsection (b) of this section for the drug which is claimed by the patent or a use of which is claimed by the patent or the representative of such holder designated to receive such notice.

(ii) The notice referred to in clause (i) shall state that an application, which contains data for bioavailability or bioequivalence studies, has been submitted under this subsection for the drug with respect to which the certification is made to obtain approval to engage in the commercial manufacture, use, or sale of such drug before

the expiration of the patent referred to in the certification. Such notice shall include a detailed statement of the factual and legal basis of the applicant's opinion that the patent is not valid or will not be infringed.

(iii) If an application is amended to include a certification described in subparagraph (A)(vii)(IV), the notice required by clause (ii) shall be given when the amended application is submitted.

(C) If a person wants to submit an abbreviated application for a new drug which has a different active ingredient or whose route of administration, dosage form, or strength differ from that of a listed drug, such person shall submit a petition to the Secretary seeking permission to file such an application. The Secretary shall approve or disapprove a petition submitted under this subparagraph within ninety days of the date the petition is submitted. The Secretary shall approve such a petition unless the Secretary finds--

(i) that investigations must be conducted to show the safety and effectiveness of the drug or of any of its active ingredients, the route of administration, the dosage form, or strength which differ from the listed drug; or

(ii) that any drug with a different active ingredient may not be adequately evaluated for approval as safe and effective on the basis of the information required to be submitted in an abbreviated application.

(3) Subject to paragraph (4), the Secretary shall approve an application for a drug unless the Secretary finds--

(A) the methods used in, or the facilities and controls used for, the manufacture, processing, and packing of the drug are inadequate to assure and preserve its identity, strength, quality, and purity;

(B) information submitted with the application is insufficient to show that each of the proposed conditions of use have been previously approved for the listed drug referred to in the application;

(C)(i) if the listed drug has only one active ingredient, information submitted with the application is insufficient to show that the active ingredient is the same as that of the listed drug;

(ii) if the listed drug has more than one active ingredient, information submitted with the application is insufficient to show that the active ingredients are the same as the active ingredients of the listed drug, or

(iii) if the listed drug has more than one active ingredient and if the application is for a drug which has an active ingredient different from the listed drug, information submitted with the application is insufficient to show--

(I) that the other active ingredients are the same as the active ingredients of the listed drug, or

(II) that the different active ingredient is an active ingredient of a listed drug or a drug which does not meet the requirements of section 321(p) of this title, or no petition to file an application for the drug with the different ingredient was approved under paragraph (2)(C);

(D)(i) if the application is for a drug whose route of administration, dosage form, or strength of the drug is the same as the route of administration, dosage form, or strength of the listed drug referred to in the application, information submitted in the application is insufficient to show that the route of administration, dosage form, or strength is the same as that of the listed drug, or

(ii) if the application is for a drug whose route of administration, dosage form, or strength of the drug is different from that of the listed drug referred to in the application, no petition to file an application for the drug with the different route of administration, dosage form, or strength was approved under paragraph (2)(C);

(E) if the application was filed pursuant to the approval of a petition under paragraph (2)(C), the application did not contain the information required by the Secretary respecting the active ingredient, route of administration, dosage form, or strength which is not the same;

(F) information submitted in the application is insufficient to show that the drug is bioequivalent to the listed drug referred to in the application or, if the

application was filed pursuant to a petition approved under paragraph (2)(C), information submitted in the application is insufficient to show that the active ingredients of the new drug are of the same pharmacological or therapeutic class as those of the listed drug referred to in paragraph (2)(A)(i) and that the new drug can be expected to have the same therapeutic effect as the listed drug when administered to patients for a condition of use referred to in such paragraph;

(G) information submitted in the application is insufficient to show that the labeling proposed for the drug is the same as the labeling approved for the listed drug referred to in the application except for changes required because of differences approved under a petition filed under paragraph (2)(C) or because the drug and the listed drug are produced or distributed by different manufacturers;

(H) information submitted in the application or any other information available to the Secretary shows that (i) the inactive ingredients of the drug are unsafe for use under the conditions prescribed, recommended, or suggested in the labeling proposed for the drug, or (ii) the composition of the drug is unsafe under such conditions because of the type of quantity of inactive ingredients included or the manner in which the inactive ingredients are included;

(I) the approval under subsection (c) of this section of the listed drug referred to in the application under this subsection has been withdrawn or suspended for

grounds described in the first sentence of subsection (e) of this section, the Secretary has published a notice of opportunity for hearing to withdraw approval of the listed drug under subsection (c) of this section for grounds described in the first sentence of subsection (e), of this section, the approval under this subsection of the listed drug referred to in the application under this subsection has been withdrawn or suspended under paragraph (5), or the Secretary has determined that the listed drug has been withdrawn from sale for safety or effectiveness reasons;

(J) the application does not meet any other requirements of paragraph (2)(A); or

(K) the application contains an untrue statement of material fact.

(4)(A) Within one hundred and eighty days of the initial receipt of an application under paragraph (2) or within such additional period as may be agreed upon by the Secretary and the applicant, the Secretary shall approve or disapprove the application.

(B) The approval of an application submitted under paragraph (2) shall made effective on the last applicable date determined under the following:

(i) If the applicant only made a certification described in subclause (I) or (II) of paragraph (2)(A)(vii) or in both such subclauses, the approval may be made effective immediately.

(ii) If the applicant made a certification described in subclause (III) of paragraph (2)(A)(vii), the approval may be made effective on the date certified under subclause (III).

(iii) If the applicant made a certification described in subclause (IV) of paragraph (2)(A)(vii), the approval shall be made effective immediately unless an action is brought for infringement of a patent which is the subject of the certification before the expiration of forty-five days from the date the notice provided under paragraph (2)(B)(i) is received. If such an action is brought before the expiration of such days, the approval shall be made effective upon the expiration of the thirty-month period beginning on the date of the receipt of the notice provided under paragraph (2)(B)(i) or such shorter or longer period as the court may order because either party to the action failed to reasonably cooperate in expediting the action, except that--

(I) if before the expiration of such period the court decides that such patent is invalid or not infringed, the approval shall be made effective on the date of the court decision,

(II) if before the expiration of such period the court decides that such patent has been infringed, the approval shall be made effective on such date as the court orders under section 271(e)(4)(A) of Title 35, or

(III) if before the expiration of such period the court grants a preliminary injunction prohibiting the

applicant from engaging in the commercial manufacture or sale of the drug until the court decides the issues of patent validity and infringement and if the court decides that such patent is invalid or not infringed, the approval shall be made effective on the date of such court decision.

In such an action, each of the parties shall reasonably cooperate in expediting the action. Until the expiration of forty-five days from the date the notice made under paragraph (2)(B)(i) is received, no action may be brought under section 2201 of title 28, United States Code, for a declaratory judgment with respect to the patent. Any action brought under section 2201 shall be brought in the judicial district where the defendant has its principal place of business or a regular and established place of business.

(iv) If the application contains a certification described in subclause (IV) of paragraph (2)(A)(vii) and is for a drug for which a previous application has been submitted under this subsection continuing such a certification, the application shall be made effective not earlier than one hundred and eighty days after--

(I) the date the Secretary receives notice from the applicant under the previous application of the first commercial marketing of the drug under the previous application, or

(II) the date of a decision of a court in an action described in clause (iii) holding the patent which is the

subject of the certification to be invalid or not infringed,

whichever is earlier.

(C) If the Secretary decides to disapprove an application, the Secretary shall give the applicant notice of an opportunity for a hearing before the Secretary on the question of whether such application is approvable. If the applicant elects to accept the opportunity for hearing by written request within thirty days after such notice, such hearing shall commence not more than ninety days after the expiration of such thirty days unless the Secretary and the applicant otherwise agree. Any such hearing shall thereafter be conducted on an expedited basis and the Secretary's order thereon shall be issued within ninety days after the date fixed by the Secretary for filing final briefs.

(D)(i) If an application (other than an abbreviated new drug application) submitted under subsection (b) of this section for a drug, no active ingredient (including any ester or sale of the active ingredient) of which has been approved in any other application under subsection (b) of this section, was approved during the period beginning January 1, 1982, and ending on September 24, 1984, the Secretary may not make the approval of an application submitted under this subsection which refers to the drug for which the subsection (b) application was submitted effective before the expiration of ten years from the date of the approval of the application under subsection (b) of this section.

(ii) If an application submitted under subsection (b) of this section for a drug, no active ingredient (including any ester or salt of the active ingredient) of which has been approved in any other application under subsection (b) of this section, is approved after September 24, 1984, no application may be submitted under this subsection which refers to the drug for which the subsection (b) application was submitted before the expiration of five years from the date of the approval of the application under subsection (b) of this section, except that such an application may be submitted under this subsection after the expiration of four years from the date of the approval of the subsection (b) application if it contains a certification of patent invalidity or noninfringement described in subclause (IV) of paragraph (2)(A)(vii). The approval of such an application shall be made effective in accordance with subparagraph (B) except that, if an action for patent infringement is commenced during the one-year period beginning forty-eight months after the date of the approval of the subsection (b) application, the thirty-month period referred to in subparagraph (B)(iii) shall be extended by such amount of time (if any) which is required for seven and one-half years to have elapsed from the date of approval of the subsection (b) application.

(iii) If an application submitted under subsection (b) of this section for a drug, which includes an active ingredient (including any ester or salt of the active ingredient) that has been approved in another application approved under subsection (b) of this section, is approved after September 24, 1984, and if such application contains reports of new clinical investigations (other than bioavailability studies)

essential to the approval of the application and conducted or sponsored by the applicant, the Secretary may not make the approval of an application submitted under this subsection for the conditions of approval of such drug in the subsection (b) application effective before the expiration of three years from the date of the approval of the application under subsection (b) of this section for such drug.

(iv) If a supplement to an application approved under subsection (b) of this section is approved after September 24, 1984, and the supplement contains reports of new clinical investigations (other than bioavailability studies) essential to the approval of the supplement and conducted or sponsored by the person submitting the supplement, the Secretary may not make the approval of an application submitted under this subsection for a change approved in the supplement effective before the expiration of three years from the date of the approval of the supplement under subsection (b) of this section.

(v) If an application (or supplement to an application) submitted under subsection (b) of this section for a drug, which includes an active ingredient (including any ester or salt of the active ingredient) that has been approved in another application under subsection (b) of this section, was approved during the period beginning January 1, 1982, and ending on September 24, 1984, the Secretary may not make the approval of an application submitted under this subsection which refers to the drug for which the subsection (b) application was submitted or which refers to a change approved in a supplement to the subsection (b)

application effective before the expiration of two years from September 24, 1984.

(5) If a drug approved under this subsection refers in its approved application to a drug the approval of which was withdrawn or suspended for grounds described in the first sentence of subsection (e) of this section or was withdrawn or suspended under this paragraph or which, as determined by the Secretary, has been withdrawn from sale for safety or effectiveness reasons, the approval of the drug under this subsection shall be withdrawn or suspended--

(A) for the same period as the withdrawal or suspension under subsection (e) of this section or this paragraph, or

(B) if the listed drug has been withdrawn from sale, for the period of withdrawal from sale or, if earlier, the period ending on the date the Secretary determines that the withdrawal from sale is not for safety or effectiveness reasons.

(6)(A)(i) Within sixty days of September 24, 1984, the Secretary shall publish and make available to the public--

(I) a list in alphabetical order of the official and proprietary name of each drug which has been approved for safety and effectiveness under subsection (c) of this section before September 24, 1984;

(II) the date of approval if the drug is approved after 1981 and the number of the application which was approved; and

(III) whether in vitro or in vivo bioequivalence studies, or both such studies, are required for applications filed under this subsection which will refer to the drug published.

(ii) Every thirty days after the publication of the first list under clause (i) the Secretary shall revise the list to include each drug which has been approved for safety and effectiveness under subsection (c) of this section or approved under this subsection during the thirty-day period.

(iii) When patent information submitted under subsection (b) or (c) of this section respecting a drug included on the list is to be published by the Secretary, the Secretary shall, in revisions made under clause (ii), include such information for such drug.

(B) A drug approved for safety and effectiveness under subsection (c) or approved under this subsection shall, for purposes of this subsection, be considered to have been published under subparagraph (A) on the date of its approval or September 24, 1984, whichever is later.

(C) If the approval of a drug was withdrawn or suspended for grounds described in the first sentence of subsection (e) of this section or was withdrawn or suspended under paragraph (5) or if the Secretary

determines that a drug has been withdrawn from sale for safety or effectiveness reasons, it may not be published in the list under subparagraph (A) or, if the withdrawal or suspension occurred after its publication in such list, it shall be immediately removed from such list--

(i) for the same period as the withdrawal or suspension under subsection (e) of this section or paragraph (5), or

(ii) if the listed drug has been withdrawn from sale, for the period of withdrawal from sale or, if earlier, the period ending on the date the Secretary determines that the withdrawal from sale is not for safety or effectiveness reasons.

A notice of the removal shall be published in the Federal Register.

(7) For purposes of this subsection:

(A) The term "bioavailability" means the rate and extent to which the active ingredient or therapeutic ingredient is absorbed from a drug and becomes available at the site of drug action.

(B) A drug shall be considered to be bioequivalent to a listed drug if--

(i) the rate and extent of absorption of the drug do not show a significant difference from the rate and extent of absorption of the listed drug when

administered at the same molar dose of the therapeutic ingredient under similar experimental conditions in either a single dose or multiple doses; or

(ii) the extent of absorption of the drug does not show a significant difference from the extent of absorption of the listed drug when administered at the same molar dose of the therapeutic ingredient under similar experimental conditions in either a single dose or multiple doses and the difference from the listed drug in the rate of absorption of the drug is intentional, is reflected in its proposed labeling, is not essential to the attainment of effective body drug concentrations on chronic use, and is considered medically insignificant for the drug.

(8) The Secretary shall, with respect to each application submitted under this subsection, maintain a record of--

(A) the name of the applicant,

(B) the name of the drug covered by the application,

(C) the name of each person to whom the review of the chemistry of the application was assigned and the date of such assignment, and

(D) the name of each person to whom the bioequivalence review for such application was assigned and the date of such assignment.

The information the Secretary is required to maintain under this paragraph with respect to an application submitted under this subsection shall be made available to the public after the approval of such application.

(k) Records and reports; required information; regulations and orders; access to records

(1) In the case of any drug for which an approval of an application filed under subsection (b) or (j) of this section is in effect, the applicant shall establish and maintain such records, and make such reports to the Secretary, of data relating to clinical experience and other data or information, received or otherwise obtained by such applicant with respect to such drug, as the Secretary may by general regulation, or by order with respect to such application, prescribe on the basis of a finding that such records and reports are necessary in order to enable the Secretary to determine, or facilitate a determination, whether there is or may be ground for invoking subsection (e) of this section. Regulations and orders issued under this subsection and under subsection (i) of this section shall have due regard for the professional ethics of the medical profession and the interests of patients and shall provide, where the Secretary deems it to be appropriate, for the examination, upon request, by the persons to whom such regulations or orders are applicable, or similar information received or otherwise obtained by the Secretary.

(2) Every person required under this section to maintain records, and every person in charge or custody thereof,

shall, upon request of an officer or employee designated by the Secretary, permit such officer or employee at all reasonable times to have access to and copy and verify such records.

(l) Public disclosure of safety and effectiveness data

Safety and effectiveness data and information which has been submitted in an application under subsection (b) of this section for a drug and which has not previously been disclosed to the public shall be made available to the public, upon request, unless extraordinary circumstances are shown--

(1) if no work is being or will be undertaken to have the application approved,

(2) if the Secretary has determined that the application is not approvable and all legal appeals have been exhausted,

(3) If approval of the application under subsection (c) of this section is withdrawn and all legal appeals have been exhausted,

(4) if the Secretary has determined that such drug is not a new drug, or

(5) upon the effective date of the approval of the first application under subsection (j) of this section which refers to such drug or upon the date upon which the approval of an application under subsection (j) of this

section which refers to such drug could be made effective if such an application had been submitted.

(m) "Patent" defined

For purposes of this section, the term "patent" means a patent issued by the Patent and Trademark Office of the Department of Commerce.

APPENDIX R

TITLE 21 -- FOOD AND DRUGS;
REVISED AS OF APRIL 1, 1995
CHAPTER I -- FOOD AND DRUG ADMINISTRATION,
DEPARTMENT OF HEALTH AND HUMAN SERVICES
SUBCHAPTER D -- DRUGS FOR HUMAN USE
PART 314 -- APPLICATIONS FOR FDA APPROVAL
TO MARKET A NEW DRUG OR
AN ANTIBIOTIC DRUG
SUBPART B -- APPLICATIONS

21 CFR 314.50 (1995)

§ 314.50 Content and format of an application.

Applications and supplements to approved applications are required to be submitted in the form and contain the information, as appropriate for the particular submission, required under this section. Three copies of the application are required: An archival copy, a review copy, and a field copy. An application for a new chemical entity will generally contain an application form, an index, a summary, five or six technical sections, case report tabulations of patient data, case report forms, drug samples, and labeling. Other applications will generally contain only some of those items, and information will be limited to that needed to support the particular submission. These include an application of the type described in section 505(b)(2) of the act, an amendment, and a supplement. The application is required to contain reports of all investigations of the drug product sponsored by the

applicant, and all other information about the drug pertinent to an evaluation of the application that is received or otherwise obtained by the applicant from any source. FDA will maintain guidelines on the format and content of applications to assist applicants in their preparation.

(a) *Application form.* The applicant shall submit a completed and signed application form that contains the following:

(1) The name and address of the applicant; the date of the application; the application number if previously issued (for example, if the application is a resubmission, an amendment, or a supplement); the name of the drug product, including its established, proprietary, code, and chemical names; the dosage form and strength; the route of administration; the identification numbers of all investigational new drug applications that are referenced in the application; the identification numbers of all drug master files and other applications under this part that are referenced in the application; and the drug product's proposed indications for use.

(2) A statement whether the submission is an original submission, a 505(b)(2) application, a resubmission, or a supplement to an application under § 314.70.

(3) A statement whether the applicant proposes to market the drug product as a prescription or an over-the-counter product.

(4) A check-list identifying what enclosures required under this section the applicant is submitting.

(5) The applicant, or the applicant's attorney, agent, or other authorized official shall sign the application. If the person signing the application does not reside or have a place of business within the United States, the application is required to contain the name and address of, and be countersigned by, an attorney, agent, or other authorized official who resides or maintains a place of business within the United States.

(b) *Index.* The archival copy of the application is required to contain a comprehensive index by volume number and page number to the summary under paragraph (c) of this section, the technical sections under paragraph (d) of this section, and the supporting information under paragraph (f) of this section.

(c) *Summary.* (1) An application is required to contain a summary of the application in enough detail that the reader may gain a good general understanding of the data and information in the application, including an understanding of the quantitative aspects of the data. The summary is not required for supplements under § 314.70. Resubmissions of an application should contain an updated summary, as appropriate. The summary should discuss all aspects of the application, and synthesize the information into a well-structured and unified document. The summary should be written at approximately the level of detail required for publication in, and meet the editorial standards generally applied by, refereed scientific and medical

journals. In addition to the agency personnel reviewing the summary in the context of their review of the application, FDA may furnish the summary to FDA advisory committee members and agency officials whose duties require an understanding of the application. To the extent possible, data in the summary should be presented in tabular and graphic forms. FDA has prepared a guideline under § 10.90(b) that provides information about how to prepare a summary. The summary required under this paragraph may be used by FDA or the applicant to prepare the Summary Basis of Approval document for public disclosure (under § 314.430(e)(2)(ii)) when the application is approved.

(2) The summary is required to contain the following information:

(i) The proposed text of the labeling for the drug, with annotations to the information in the summary and technical sections of the application that support the inclusion of each statement in the labeling, and, if the application is for a prescription drug, statements describing the reasons for omitting a section or subsection of the labeling format in § 201.57.

(ii) A statement identifying the pharmacologic class of the drug and a discussion of the scientific rationale for the drug, its intended use, and the potential clinical benefits of the drug product.

(iii) A brief description of the marketing history, if any, of the drug outside the United States, including a list of the

countries in which the drug has been marketed, a list of any countries in which the drug has been withdrawn from marketing for any reason related to safety or effectiveness, and a list of countries in which applications for marketing are pending. The description is required to describe both marketing by the applicant and, if known, the marketing history of other persons.

(iv) A summary of the chemistry, manufacturing, and controls section of the application.

(v) A summary of the nonclinical pharmacology and toxicology section of the application.

(vi) A summary of the human pharmacokinetics and bioavailability section of the application.

(vii) A summary of the microbiology section of the application (for anti-infective drugs only).

(viii) A summary of the clinical data section of the application, including the results of statistical analyses of the clinical trials.

(ix) A concluding discussion that presents the benefit and risk considerations related to the drug, including a discussion of any proposed additional studies or surveillance the applicant intends to conduct postmarketing.

(d) *Technical sections.* The application is required to contain the technical sections described below. Each technical section is required to contain data and

information in sufficient detail to permit the agency to make a knowledgeable judgment about whether to approve the application or whether grounds exist under section 505(d) or 507 of the act to refuse to approve the application. The required technical sections are as follows:

(1) *Chemistry, manufacturing, and controls section.* A section describing the composition, manufacture, and specification of the drug substance and the drug product, including the following:

(i) *Drug substance.* A full description of the drug substance including its physical and chemical characteristics and stability; the name and address of its manufacturer; the method of synthesis (or isolation) and purification of the drug substance; the process controls used during manufacture and packaging; and such specifications and analytical methods as are necessary to assure the identity, strength, quality, and purity of the drug substance and the bioavailability of the drug products made from the substance, including, for example, specifications relating to stability, sterility, particle size, and crystalline form. The application may provide additionally for the use of alternatives to meet any of these requirements, including alternative sources, process controls, methods, and specifications. Reference to the current edition of the U.S. Pharmacopeia and the National Formulary may satisfy relevant requirements in this paragraph.

(ii)(a) *Drug product.* A list of all components used in the manufacture of the drug product (regardless of whether they appear in the drug product); and a statement of the

composition of the drug product; a statement of the specifications and analytical methods for each component; the name and address of each manufacturer the drug product; a description of the manufacturing and packaging procedures and in-process controls for the drug product; such specifications and analytical methods as are necessary to assure the identity, strength, quality, purity, and bioavailability of the drug product, including, for example, specifications relating to sterility, dissolution rate, containers and closure systems; and stability data with proposed expiration dating. The application may provide additionally for the use of alternatives to meet any of these requirements, including alternative components, manufacturing and packaging procedures, in-process controls, methods, and specifications. Reference to the current edition of the U.S. Pharmacopeia and the National Formulary may satisfy relevant requirements in this paragraph.

(b) Unless provided by paragraph (d)(1)(ii)(a) of this section, for each batch of the drug product used to conduct a bioavailability or bioequivalence study described in § 320.38 or § 320.63 of this chapter or used to conduct a primary stability study: The batch production record; the specifications and test procedures for each component and for the drug product; the names and addresses of the sources of the active and noncompendial inactive components and of the container and closure system for the drug product; the name and address of each contract facility involved in the manufacture, processing, packaging, or testing of the drug product and identification of the operation performed by each contract facility; and the

results of any test performed on the components used in the manufacture of the drug product as required by § 211.84(d) of this chapter and on the drug product as required by § 211.165 of this chapter.

(c) The proposed or actual master production record, including a description of the equipment, to be used for the manufacture of a commercial lot of the drug product or a comparably detailed description of the production process for a representative batch of the drug product.

(iii) Environmental impact. The application is required to contain either a claim for categorical exclusion under § 25.24 of this chapter or an environmental assessment under § 25.31 of this chapter.

(iv) The applicant may, at its option, submit a complete chemistry, manufacturing, and controls section 90 to 120 days before the anticipated submission of the remainder of the application. FDA will review such early submissions as resources permit.

(v) Except for a foreign applicant, the applicant shall include a statement certifying that the field copy of the application has been provided to the applicant's home FDA district office.

(2) *Nonclinical pharmacology and toxicology section.* A section describing, with the aid of graphs and tables, animal and in vitro studies with drug, including the following:

(i) Studies of the pharmacological actions of the drug in relation to its proposed therapeutic indication and studies that otherwise define the pharmacologic properties of the drug or are pertinent to possible adverse effects.

(ii) Studies of the toxicological effects of the drug as they relate to the drug's intended clinical uses, including, as appropriate, studies assessing the drug's acute, subacute, and chronic toxicity; carcinogenicity; and studies of toxicities related to the drug's particular mode of administration or conditions of use.

(iii) Studies, as appropriate, of the effects of the drug on reproduction and on the developing fetus.

(iv) Any studies of the absorption, distribution, metabolism, and excretion of the drug in animals.

(v) For each nonclinical laboratory study subject to the good laboratory practice regulations under part 58 a statement that it was conducted in compliance with the good laboratory practice regulations in part 58, or, if the study was not conducted in compliance with those regulations, a brief statement of the reason for the noncompliance.

(3) *Human pharmacokinetics and bioavailability section.* A section describing the human pharmacokinetic data and human bioavailability data, or information supporting a waiver of the submission of in vivo bioavailability data under subpart B of part 320, including the following:

(i) A description of each of the bioavailability and pharmacokinetic studies of the drug in humans performed by or on behalf of the applicant that includes a description of the analytical and statistical methods used in each study and a statement with respect to each study that it either was conducted in compliance with the institutional review board regulations in part 56, or was not subject to the regulations under § 56.104 or § 56.105, and that it was conducted in compliance with the informed consent regulations in part 50.

(ii) If the application describes in the chemistry, manufacturing, and controls section specifications or analytical methods needed to assure the bioavailability of the drug product or drug substance, or both, a statement in this section of the rationale for establishing the specification or analytical methods, including data and information supporting the rationale.

(iii) A summarizing discussion and analysis of the pharmacokinetics and metabolism of the active ingredients and the bioavailability or bioequivalence, or both, of the drug product.

(4) *Microbiology section.* If the drug is an anti-infective drug, a section describing the microbiology data, including the following:

(i) A description of the biochemical basis of the drug's action on microbial physiology.

(ii) A description of the antimicrobial spectra of the drug, including results of in vitro preclinical studies to demonstrate concentrations of the drug required for effective use.

(iii) A description of any known mechanisms of resistance to the drug, including results of any known epidemiologic studies to demonstrate prevalence of resistance factors.

(iv) A description of clinical microbiology laboratory methods (for example, in vitro sensitivity discs) needed for effective use of the drug.

(5) *Clinical data section.* A section describing the clinical investigations of the drug, including the following:

(i) A description and analysis of each clinical pharmacology study of the drug, including a brief comparison of the results of the human studies with the animal pharmacology and toxicology data.

(ii) A description and analysis of each controlled clinical study pertinent to a proposed use of the drug, including the protocol and a description of the statistical analyses used to evaluate the study. If the study report is an interim analysis, this is to be noted and a projected completion date provided. Controlled clinical studies that have not been analyzed in detail for any reason (e.g., because they have been discontinued or are incomplete) are to be included in this section, including a copy of the

protocol and a brief description of the results and status of the study.

(iii) A description of each uncontrolled clinical study, a summary of the results, and a brief statement explaining why the study is classified as uncontrolled.

(iv) A description and analysis of any other data or information relevant to an evaluation of the safety and effectiveness of the drug product obtained or otherwise received by the applicant from any source, foreign or domestic, including information derived from clinical investigations, including controlled and uncontrolled studies of uses of the drug other than those proposed in the application, commercial marketing experience, reports in the scientific literature, and unpublished scientific papers.

(v) An integrated summary of the data demonstrating substantial evidence of effectiveness for the claimed indications. Evidence is also required to support the dosage and administration section of the labeling, including support for the dosage and dose interval recommended, and modifications for specific subgroups (for example, pediatrics, geriatrics, patients with renal failure).

(vi) A summary and updates of safety information, as follows:

(a) The applicant shall submit an integrated summary of all available information about the safety of the drug product, including pertinent animal data, demonstrated or potential adverse effects of the drug, clinically significant

drug/drug interactions, and other safety considerations, such as data from epidemiological studies of related drugs. A description of any statistical analyses performed in analyzing safety data should also be included, unless already included under paragraph (d)(5)(ii) of this section.

(b) The applicant shall, under section 505(i) of the act, update periodically its pending application with new safety information learned about the drug that may reasonably affect the statement of contraindications, warnings, precautions, and adverse reactions in the draft labeling. These "safety update reports" are required to include the same kinds of information (from clinical studies, animal studies, and other sources) and are required to be submitted in the same format as the integrated summary in paragraph (d)(5)(vi)(a) of this section. In addition, the reports are required to include the case report forms for each patient who died during a clinical study or who did not complete the study because of an adverse event (unless this requirement is waived). The applicant shall submit these reports (1) 4 months after the initial submission; (2) following receipt of an approvable letter; and (3) at other times as requested by FDA. Prior to the submission of the first such report, applicants are encouraged to consult with FDA regarding further details on its form and content.

(vii) If the drug has a potential for abuse, a description and analysis of studies or information related to abuse of the drug, including a proposal for scheduling under the Controlled Substances Act. A description of any studies related to overdosage is also required, including

information on dialysis, antidotes, or other treatments, if known.

(viii) An integrated summary of the benefits and risks of the drug, including a discussion of why the benefits exceed the risks under the conditions stated in the labeling.

(ix) A statement with respect to each clinical study involving human subjects that it either was conducted in compliance with the institutional review board regulations in part 56, or was not subject to the regulations under § 56.104 or § 56.105, and that it was conducted in compliance with the informed consent regulations in part 50.

(x) If a sponsor has transferred any obligations for the conduct of any clinical study to a contract research organization, a statement containing the name and address of the contract research organization, identification of the clinical study, and a listing of the obligations transferred. If all obligations governing the conduct of the study have been transferred, a general statement of this transfer -- in lieu of a listing of the specific obligations transferred -- may be submitted.

(xi) If original subject records were audited or reviewed by the sponsor in the course of monitoring any clinical study to verify the accuracy of the case reports submitted to the sponsor, a list identifying each clinical study so audited or reviewed.

(6) *Statistical section.* A section describing the statistical evaluation of clinical data, including the following:

(i) A copy of the information submitted under paragraph (d)(5)(ii) of this section concerning the description and analysis of each controlled clinical study, and the documentation and supporting statistical analyses used in evaluating the controlled clinical studies.

(ii) A copy of the information submitted under paragraph (d)(5)(vi)(a) of this section concerning a summary of information about the safety of the drug product, and the documentation and supporting statistical analyses used in evaluating the safety information.

(e) *Samples and labeling.* (1) Upon request from FDA, the applicant shall submit the samples described below to the places identified in the agency's request. FDA will generally ask applicants to submit samples directly to two or more agency laboratories that will perform all necessary tests on the samples and validate the applicant's analytical methods.

(i) Four representative samples of the following, each sample in sufficient quantity to permit FDA to perform three times each test described in the application to determine whether the drug substance and the drug product meet the specifications given in the application:

(a) The drug product proposed for marketing;

(b) The drug substance used in the drug product from which the samples of the drug product were taken; and

(c) Reference standards and blanks (except that reference standards recognized in an official compendium need not be submitted).

(ii) Samples of the finished market package, if requested by FDA.

(2) The applicant shall submit the following in the archival copy of the application:

(i) Three copies of the analytical methods and related descriptive information contained in the chemistry, manufacturing, and controls section under paragraph (d)(1) of this section for the drug substance and the drug product that are necessary for FDA's laboratories to perform all necessary tests on the samples and to validate the applicant's analytical methods. The related descriptive information includes a description of each sample; the proposed regulatory specifications for the drug; a detailed description of the methods of analysis; supporting data for accuracy, specificity, precision and ruggedness; and complete results of the applicant's tests on each sample.

(ii) Copies of the label and all labeling for the drug product (4 copies of draft labeling or 12 copies of final printed labeling).

(f) *Case report forms and tabulations.* The archival copy of the application is required to contain the following case report tabulations and case report forms:

(1) *Case report tabulations.* The application is required to contain tabulations of the data from each adequate and well-controlled study under § 314.126 (Phase 2 and Phase 3 studies as described in §§ 312.21 (b) and (c) of this chapter), tabulations of the data from the earliest clinical pharmacology studies (Phase 1 studies as described in § 312.21(a) of this chapter), and tabulations of the safety data from other clinical studies. Routine submission of other patient data from uncontrolled studies is not required. The tabulations are required to include the data on each patient in each study, except that the applicant may delete those tabulations which the agency agrees, in advance, are not pertinent to a review of the drug's safety or effectiveness. Upon request, FDA will discuss with the applicant in a "pre-NDA" conference those tabulations that may be appropriate for such deletion. Barring unforeseen circumstances, tabulations agreed to be deleted at such a conference will not be requested during the conduct of FDA's review of the application. If such unforeseen circumstances do occur, any request for deleted tabulations will be made by the director of the FDA division responsible for reviewing the application, in accordance with paragraph (f)(3) of this section.

(2) *Case report forms.* The application is required to contain copies of individual case report forms for each patient who died during a clinical study or who did not complete the study because of an adverse event, whether

believed to be drug related or not, including patients receiving reference drugs or placebo. This requirement may be waived by FDA for specific studies if the case report forms are unnecessary for a proper review of the study.

(3) *Additional data.* The applicant shall submit to FDA additional case report forms and tabulations needed to conduct a proper review of the application, as requested by the director of the FDA division responsible for reviewing the application. The applicant's failure to submit information requested by FDA within 30 days after receipt of the request may result in the agency viewing any eventual submission as a major amendment under § 314.60 and extending the review period as necessary. If desired by the applicant, the FDA division director will verify in writing any request for additional data that was made orally.

(4) Applicants are invited to meet with FDA before submitting an application to discuss the presentation and format of supporting information. If the applicant and FDA agree, the applicant may submit tabulations of patient data and case report forms in a form other than hard copy, for example, on microfiche or computer tapes.

(g) *Other.* The following general requirements apply to the submission of information within the summary under paragraph (c) of this section and within the technical sections under paragraph (d) of this section.

(1) The applicant ordinarily is not required to resubmit information previously submitted, but may incorporate the

information by reference. A reference to information submitted previously is required to identify the file by name, reference number, volume, and page number in the agency's records where the information can be found. A reference to information submitted to the agency by a person other than the applicant is required to contain a written statement that authorizes the reference and that is signed by the person who submitted the information.

(2) The applicant shall submit an accurate and complete English translation of each part of the application that is not in English. The applicant shall submit a copy of each original literature publication for which an English translation is submitted.

(3) If an applicant who submits a new drug application under section 505(b) of the act obtains a "right of reference or use," as defined under § 314.3(b), to an investigation described in clause (A) of section 505(b)(1) of the act, the applicant shall include in its application a written statement signed by the owner of the data from each such investigation that the applicant may rely on in support of the approval of its application, and provide FDA access to, the underlying raw data that provide the basis for the report of the investigation submitted in its application.

(h) *Patent information.* The application is required to contain the patent information described under § 314.53.

(i) *Patent certification* -- (1) *Contents.* A 505(b)(2) application is required to contain the following:

(i) *Patents claiming drug, drug product, or method of use.* (A) Except as provided in paragraph (i)(2) of this section, a certification with respect to each patent issued by the United States Patent and Trademark Office that, in the opinion of the applicant and to the best of its knowledge, claims a drug (the drug product or drug substance that is a component of the drug product) on which investigations that are relied upon by the applicant for approval of its application were conducted or that claims an approved use for such drug and for which information is required to be filed under section 505(b) and (c) of the act and § 314.53. For each such patent, the applicant shall provide the patent number and certify, in its opinion and to the best of its knowledge, one of the following circumstances:

(1) That the patent information has not been submitted to FDA. The applicant shall entitle such a certification "Paragraph I Certification";

(2) That the patent has expired. The applicant shall entitle such a certification "Paragraph II Certification";

(3) The date on which the patent will expire. The applicant shall entitle such a certification "Paragraph III Certification"; or

(4) That the patent is invalid, unenforceable, or will not be infringed by the manufacture, use, or sale of the drug product for which the application is submitted. The applicant shall entitle such a certification "Paragraph IV Certification". This certification shall be submitted in the following form:

I, *(name of applicant)*, certify that Patent No._____ *(is invalid, unenforceable, or will not be infringed by the manufacture, use, or sale of) (name of proposed drug product)* for which this application is submitted.

The certification shall be accompanied by a statement that the applicant will comply with the requirements under § 314.52(a) with respect to providing a notice to each owner of the patent or their representatives and to the holder of the approved application for the drug product which is claimed by the patent or a use of which is claimed by the patent and with the requirements under § 314.52(c) with respect to the content of the notice.

(B) If the drug on which investigations that are relied upon by the applicant were conducted is itself a licensed generic drug of a patented drug first approved under section 505(b) of the act, the appropriate patent certification under this section with respect to each patent that claims the first-approved patented drug or that claims an approved use for such a drug.

(ii) *No relevant patents.* If, in the opinion of the applicant and to the best of its knowledge, there are no patents described in paragraph (i)(1)(i) of this section, a certification in the following form:

In the opinion and to the best knowledge of *(name of applicant)*, there are no patents that claim the drug or drugs on which investigations that are relied upon in this application were conducted or that claim a use of such drug or drugs.

(iii) *Method of use patent.* (A) If information that is submitted under section 505(b) or (c) of the act and § 314.53 is for a method of use patent, and the labeling for the drug product for which the applicant is seeking approval does not include any indications that are covered by the use patent, a statement explaining that the method of use patent does not claim any of the proposed indications.

(B) If the labeling of the drug product for which the applicant is seeking approval includes an indication that, according to the patent information submitted under section 505(b) or (c) of the act and § 314.53 or in the opinion of the applicant, is claimed by a use patent, the applicant shall submit an applicable certification under paragraph (i)(1)(i) of this section.

(2) *Method of manufacturing patent.* An applicant is not required to make a certification with respect to any patent that claims only a method of manufacturing the drug product for which the applicant is seeking approval.

(3) *Licensing agreements.* If a 505(b)(2) application is for a drug or method of using a drug claimed by a patent and the applicant has a licensing agreement with the patent owner, the applicant shall submit a certification under

paragraph (i)(1)(i)(A)(4) of this section ("Paragraph IV Certification") as to that patent and a statement that it has been granted a patent license. If the patent owner consents to an immediate effective date upon approval of the 505(b)(2) application, the application shall contain a written statement from the patent owner that it has a licensing agreement with the applicant and that it consents to an immediate effective date.

(4) *Late submission of patent information.* If a patent described in paragraph (i)(1)(i)(A) of this section is issued and the holder of the approved application for the patented drug does not submit the required information on the patent within 30 days of issuance of the patent, an applicant who submitted a 505(b)(2) application that, before the submission of the patent information, contained an appropriate patent certification is not required to submit an amended certification. An applicant whose 505(b)(2) application is filed after a late submission of patent information or whose 505(b)(2) application was previously filed but did not contain an appropriate patent certification at the time of the patent submission shall submit a certification under paragraph (i)(1)(i) or (i)(1)(ii) of this section or a statement under paragraph (i)(1)(iii) of this section as to that patent.

(5) *Disputed patent information.* If an applicant disputes the accuracy or relevance of patent information submitted to FDA, the applicant may seek a confirmation of the correctness of the patent information in accordance with the procedures under § 314.53(f). Unless the patent

information is withdrawn or changed, the applicant must submit an appropriate certification for each relevant patent.

(6) *Amended certifications.* A certification submitted under paragraphs (i)(1)(i) through (i)(1)(iii) of this section may be amended at any time before the effective date of the approval of the application. An applicant shall submit an amended certification as an amendment to a pending application or by letter to an approved application. If an applicant with a pending application voluntarily makes a patent certification for an untimely filed patent, the applicant may withdraw the patent certification for the untimely filed patent. Once an amendment or letter for the change in certification has been submitted, the application will no longer be considered to be one containing the prior certification.

(i) *After finding of infringement.* An applicant who has submitted a certification under paragraph (i)(1)(i)(A)(4) of this section and is sued for patent infringement within 45 days of the receipt of notice sent under § 314.52 shall amend the certification if a final judgment in the action is entered finding the patent to be infringed unless the final judgment also finds the patent to be invalid. In the amended certification, the applicant shall certify under paragraph (i)(1)(i)(A)(3) of this section that the patent will expire on a specific date.

(ii) *After removal of a patent from the list.* If a patent is removed from the list, any applicant with a pending application (including a tentatively approved application with a delayed effective date) who has made a certification

with respect to such patent shall amend its certification. The applicant shall certify under paragraph (i)(1)(ii) of this section that no patents described in paragraph (i)(1)(i) of this section claim the drug or, if other relevant patents claim the drug, shall amend the certification to refer only to those relevant patents. In the amendment, the applicant shall state the reason for the change in certification (that the patent is or has been removed from the list). A patent that is the subject of a lawsuit under § 314.107(c) shall not be removed from the list until FDA determines either that no delay in effective dates of approval is required under that section as a result of the lawsuit, that the patent has expired, or that any such period of delay in effective dates of approval is ended. An applicant shall submit an amended certification as an amendment to a pending application. Once an amendment for the change has been submitted, the application will no longer be considered to be one containing a certification under paragraph (i)(1)(i)(A)(4) of this section.

(iii) *Other amendments*. (A) Except as provided in paragraphs (i)(4) and (i)(6)(iii)(B) of this section, an applicant shall amend a submitted certification if, at any time before the effective date of the approval of the application, the applicant learns that the submitted certification is no longer accurate.

(B) An applicant is not required to amend a submitted certification when information on an otherwise applicable patent is submitted after the effective date of approval for the 505(b)(2) application.

(j) *Claimed exclusivity.* A new drug product, upon approval, may be entitled to a period of marketing exclusivity under the provisions of § 314.108. If an applicant believes its drug product is entitled to a period of exclusivity, it shall submit with the new drug application prior to approval the following information:

(1) A statement that the applicant is claiming exclusivity.

(2) A reference to the appropriate paragraph under § 314.108 that supports its claim.

(3) If the applicant claims exclusivity under § 314.108(b)(2), information to show that, to the best of its knowledge or belief, a drug has not previously been approved under section 505(b) of the act containing any active moiety in the drug for which the applicant is seeking approval.

(4) If the applicant claims exclusivity under § 314.108(b)(4) or (b)(5), the following information to show that the application contains "new clinical investigations" that are "essential to approval of the application or supplement" and were "conducted or sponsored by the applicant:"

(i) *"New clinical investigations."* A certification that to the best of the applicant's knowledge each of the clinical investigations included in the application meets the definition of "new clinical investigation" set forth in § 314.108(a).

(ii) *"Essential to approval."* A list of all published studies or publicly available reports of clinical investigations known to the applicant through a literature search that are relevant to the conditions for which the applicant is seeking approval, a certification that the applicant has thoroughly searched the scientific literature and, to the best of the applicant's knowledge, the list is complete and accurate and, in the applicant's opinion, such published studies or publicly available reports do not provide a sufficient basis for the approval of the conditions for which the applicant is seeking approval without reference to the new clinical investigation(s) in the application, and an explanation as to why the studies or reports are insufficient.

(iii) *"Conducted or sponsored by."* If the applicant was the sponsor named in the Form FDA-1571 for an investigational new drug application (IND) under which the new clinical investigation(s) that is essential to the approval of its application was conducted, identification of the IND by number. If the applicant was not the sponsor of the IND under which the clinical investigation(s) was conducted, a certification that the applicant or its predecessor in interest provided substantial support for the clinical investigation(s) that is essential to the approval of its application, and information supporting the certification. To demonstrate "substantial support," an applicant must either provide a certified statement from a certified public accountant that the applicant provided 50 percent or more of the cost of conducting the study or provide an explanation of why FDA should consider the applicant to have conducted or sponsored the study if the applicant's

financial contribution to the study is less than 50 percent or the applicant did not sponsor the investigational new drug. A predecessor in interest is an entity, e.g., a corporation, that the applicant has taken over, merged with, or purchased, or from which the applicant has purchased all rights to the drug. Purchase of nonexclusive rights to a clinical investigation after it is completed is not sufficient to satisfy this definition.

(k) *Format of an original application.* (1) The applicant shall submit a complete archival copy of the application that contains the information required under paragraphs (a) through (f) of this section. FDA will maintain the archival copy during the review of the application to permit individual reviewers to refer to information that is not contained in their particular technical sections of the application, to give other agency personnel access to the application for official business, and to maintain in one place a complete copy of the application. An applicant may submit on microfiche the portions of the archival copy of the application described in paragraphs (b) through (d) of this section. Information relating to samples and labeling, described in paragraph (e) of this section, is required to be submitted in hard copy. Tabulations of patient data and case report forms, described in paragraph (f) of this section, may be submitted on microfiche only if the applicant and FDA agree. If FDA agrees, the applicant may use another suitable microform system.

(2) The applicant shall submit a review copy of the application. Each of the technical sections, described in

paragraphs (d)(1) through (d)(6) of this section, in the review copy is required to be separately bound with a copy of the application form required under paragraph (a) of this section and a copy of the summary required under paragraph (c) of this section.

(3) The applicant shall submit a field copy of the application that contains the technical section described in paragraph (d)(1) of this section, a copy of the application form required under paragraph (a) of this section, a copy of the summary required under paragraph (c) of this section, and a certification that the field copy is a true copy of the technical section described in paragraph (d)(1) of this section contained in the archival and review copies of the application.

(4) The applicant may obtain from FDA sufficient folders to bind the archival, the review, and the field copies of the application.

(Collection of information requirements approved by the Office of Management and Budget under control number 0910-0001)

APPENDIX S

TITLE 21 -- FOOD AND DRUGS;
REVISED AS OF APRIL 1, 1995
CHAPTER I -- FOOD AND DRUG ADMINISTRATION,
DEPARTMENT OF HEALTH AND HUMAN SERVICES
SUBCHAPTER D -- DRUGS FOR HUMAN USE
PART 314 -- APPLICATIONS FOR FDA APPROVAL
TO MARKET A NEW DRUG
OR AN ANTIBIOTIC DRUG
SUBPART B -- APPLICATIONS

21 CFR 314.53 (1995)

§ 314.53 Submission of patent information.

(a) *Who must submit patent information.* This section applies to any applicant who submits to FDA a new drug application or an amendment to it under section 505(b) of the act and § 314.50 or a supplement to an approved application under § 314.70, except as provided in paragraph (d)(2) of this section.

(b) *Patents for which information must be submitted.* An applicant described in paragraph (a) of this section shall submit information on each patent that claims the drug or a method of using the drug that is the subject of the new drug application or amendment or supplement to it and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product. For purposes of this part, such

patents consist of drug substance (ingredient) patents, drug product (formulation and composition) patents, and method of use patents. Process patents are not covered by this section and information on process patents may not be submitted to FDA. For patents that claim a drug substance or drug product, the applicant shall submit information only on those patents that claim a drug product that is the subject of a pending or approved application, or that claim a drug substance that is a component of such a product. For patents that claim a method of use, the applicant shall submit information only on those patents that claim indications or other conditions of use of a pending or approved application.

(c) *Reporting requirements* -- (1) General requirements. An applicant described in paragraph (a) of this section shall submit the following information for each patent described in paragraph (b) of this section:

(i) Patent number and the date on which the patent will expire.

(ii) Type of patent, i.e., drug, drug product, or method of use.

(iii) Name of the patent owner.

(iv) If the patent owner or applicant does not reside or have a place of business within the United States, the name of an agent (representative) of the patent owner or applicant who resides or maintains a place of business within the United States authorized to receive notice of

patent certification under section 505(b)(3) and (j)(2)(B) of the act and §§ 314.52 and 314.95.

(2) *Formulation, composition, or method of use patents* -- (i) **Original declaration**. For each formulation, composition, or method of use patent, in addition to the patent information described in paragraph (c)(1) of this section the applicant shall submit the following declaration:

> The undersigned declares that Patent No. ___ covers the formulation, composition, and/or method of use of *(name of drug product)*. This product is *(currently approved under section 505 of the Federal Food, Drug, and Cosmetic Act)* [or] *(the subject of this application for which approval is being sought)*:
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(ii) *Amendment of patent information upon approval.* Within 30 days after the date of approval of its application, if the application contained a declaration required under paragraph (c)(2)(i) of this section, the applicant shall by letter amend the declaration to identify each patent that claims the formulation, composition, or the specific indications or other conditions of use that have been approved.

(3) *No relevant patents.* If the applicant believes that there are no patents which claim the drug or the drug product or which claim a method of using the drug product and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by

the owner of the patent engaged in the manufacture, use, or sale of the drug product, it shall so declare.

(4) *Authorized signature.* The declarations required by this section shall be signed by the applicant or patent owner, or the applicant's or patent owner's attorney, agent (representative), or other authorized official.

(d) *When and where to submit patent information -- (1) Original application.* An applicant shall submit with its original application submitted under this part, including an application described in section 505(b)(2) of the act, the information described in paragraph (c) of this section on each drug (ingredient), drug product (formulation and composition), and method of use patent issued before the application is filed with FDA and for which patent information is required to be submitted under this section. If a patent is issued after the application is filed with FDA but before the application is approved, the applicant shall, within 30 days of the date of issuance of the patent, submit the required patent information in an amendment to the application under § 314.60.

(2) *Supplements.* (i) An applicant shall submit patent information required under paragraph (c) of this section for a patent that claims the drug, drug product, or method of use for which approval is sought in any of the following supplements:

(A) To change the formulation;

(B) To add a new indication or other condition of use, including a change in route of administration;

(C) To change the strength;

(D) To make any other patented change regarding the drug, drug product, or any method of use.

(ii) If the applicant submits a supplement for one of the changes listed under paragraph (d)(2)(i) of this section and existing patents for which information has already been submitted to FDA claim the changed product, the applicant shall submit a certification with the supplement identifying the patents that claim the changed product.

(iii) If the applicant submits a supplement for one of the changes listed under paragraph (d)(2)(i) of this section and no patents, including previously submitted patents, claim the changed product, it shall so certify.

(iv) The applicant shall comply with the requirements for amendment of formulation or composition and method of use patent information under paragraphs (c)(2)(ii) and (d)(3) of this section.

(3) *Patent information deadline*. If a patent is issued for a drug, drug product, or method of use after an application is approved, the applicant shall submit to FDA the required patent information within 30 days of the date of issuance of the patent.

(4) *Copies.* The applicant shall submit two copies of each submission of patent information, an archival copy and a copy for the chemistry, manufacturing, and controls section of the review copy, to the Central Document Room, Center for Drug Evaluation and Research, Food and Drug Administration, Park Bldg., rm. 2-14, 12420 Parklawn Dr., Rockville, MD 20857. The applicant shall submit the patent information by letter separate from, but at the same time as, submission of the supplement.

(5) *Submission date.* Patent information shall be considered to be submitted to FDA as of the date the information is received by the Central Document Room.

(6) *Identification.* Each submission of patent information, except information submitted with an original application, and its mailing cover shall bear prominent identification as to its contents, i.e., "Patent Information," or, if submitted after approval of an application, "Time Sensitive Patent Information."

(e) *Public disclosure of patent information.* FDA will publish in the list the patent number and expiration date of each patent that is required to be, and is, submitted to FDA by an applicant, and for each use patent, the approved indications or other conditions of use covered by a patent. FDA will publish such patent information upon approval of the application, or, if the patent information is submitted by the applicant after approval of an application as provided under paragraph (d)(2) of this section, as soon as possible after the submission to the agency of the patent information. Patent information submitted by the last

working day of a month will be published in that month's supplement to the list. Patent information received by the agency between monthly publication of supplements to the list will be placed on public display in FDA's Freedom of Information Staff. A request for copies of the file shall be sent in writing to the Freedom of Information Staff (HFI-35), Food and Drug Administration, rm. 12A-16, 5600 Fishers Lane, Rockville MD 20857.

(f) *Correction of patent information errors.* If any person disputes the accuracy or relevance of patent information submitted to the agency under this section and published by FDA in the list, or believes that an applicant has failed to submit required patent information, that person must first notify the agency in writing stating the grounds for disagreement. Such notification should be directed to the Drug Information Services Branch (HFD-84), Center for Drug Evaluation and Research, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857. The agency will then request of the applicable new drug application holder that the correctness of the patent information or omission of patent information be confirmed. Unless the application holder withdraws or amends its patent information in response to FDA's request, the agency will not change the patent information in the list. If the new drug application holder does not change the patent information submitted to FDA, a 505(b)(2) application or an abbreviated new drug application under section 505(j) of the act submitted for a drug that is claimed by a patent for which information has been submitted must, despite any disagreement as to the

correctness of the patent information, contain an appropriate certification for each listed patent.

APPENDIX T

TITLE 21 -- FOOD AND DRUGS;
REVISED AS OF APRIL 1, 1995
CHAPTER I -- FOOD AND DRUG ADMINISTRATION,
DEPARTMENT OF HEALTH AND HUMAN SERVICES
SUBCHAPTER D -- DRUGS FOR HUMAN USE
PART 314 -- APPLICATIONS FOR FDA APPROVAL
TO MARKET A NEW DRUG
OR AN ANTIBIOTIC DRUG
SUBPART C -- ABBREVIATED APPLICATIONS

21 CFR 314.94 (1995)

§ 314.94 Content and format of an abbreviated application.

Abbreviated applications are required to be submitted in the form and contain the information required under this section. Three copies of the application are required, an archival copy, a review copy, and a field copy. FDA will maintain guidelines on the format and content of applications to assist applicants in their preparation.

(a) *Abbreviated new drug applications.* Except as provided in paragraph (b) of this section, the applicant shall submit a complete archival copy of the abbreviated new drug application that includes the following:

(1) *Application form.* The applicant shall submit a completed and signed application form that contains the information described under § 314.50(a)(1), (a)(3), (a)(4),

and (a)(5). The applicant shall state whether the submission is an abbreviated application under this section or a supplement to an abbreviated application under § 314.97.

(2) *Table of contents.* the archival copy of the abbreviated new drug application is required to contain a table of contents that shows the volume number and page number of the contents of the submission.

(3) *Basis for abbreviated new drug application submission.* An abbreviated new drug application must refer to a listed drug. Ordinarily, that listed drug will be the drug product selected by the agency as the reference standard for conducting bioequivalence testing. The application shall contain:

(i) The name of the reference listed drug, including its dosage form and strength. For an abbreviated new drug application based on an approved petition under § 10.30 of this chapter or § 314.93, the reference listed drug must be the same as the listed drug approved in the petition.

(ii) A statement as to whether, according to the information published in the list, the reference listed drug is entitled to a period of marketing exclusivity under section 505(j)(4)(D) of the act.

(iii) For an abbreviated new drug application based on an approved petition under § 10.30 of this chapter or § 314.93, a reference to FDA-assigned docket number for the petition and a copy of FDA's correspondence approving the petition.

(4) *Conditions of use.* (i) A statement that the conditions of use prescribed, recommended, or suggested in the labeling proposed for the drug product have been previously approved for the reference listed drug.

(ii) A reference to the applicant's annotated proposed labeling and to the currently approved labeling for the reference listed drug provided under paragraph (a)(8) of this section.

(5) *Active ingredients.* (i) For a single-active-ingredient drug product, information to show that the active ingredient is the same as that of the reference single-active-ingredient listed drug, as follows:

(A) A statement that the active ingredient of the proposed drug product is the same as that of the reference listed drug.

(B) A reference to the applicant's annotated proposed labeling and to the currently approved labeling for the reference listed drug provided under paragraph (a)(8) of this section.

(ii) For a combination drug product, information to show that the active ingredients are the same as those of the reference listed drug except for any different active ingredient that has been the subject of an approved petition, as follows:

(A) A statement that the active ingredients of the proposed drug product are the same as those of the

reference listed drug, or if one of the active ingredients differs from one of the active ingredients of the reference listed drug and the abbreviated application is submitted under the approval of a petition under § 314.93 to vary such active ingredient, information to show that the other active ingredients of the drug product are the same as the other active ingredients of the reference listed drug, information to show that the different active ingredient is an active ingredient of another listed drug or of a drug that does not meet the definition of "new drug" in section 201(p) of the act, and such other information about the different active ingredient that FDA may require.

(B) A reference to the applicant's annotated proposed labeling and to the currently approved labeling for the reference listed drug provided under paragraph (a)(8) of this section.

(6) *Route of administration, dosage form, and strength.* (i) Information to show that the route of administration, dosage form, and strength of the drug product are the same as those of the reference listed drug except for any differences that have been the subject of an approved petition, as follows:

(A) A statement that the route of administration, dosage form, and strength of the proposed drug product are the same as those of the reference listed drug.

(B) A reference to the applicant's annotated proposed labeling and to the currently approved labeling for the

reference listed drug provided under paragraph (a)(8) of this section.

(ii) If the route of administration, dosage form, or strength of the drug product differs from the reference listed drug and the abbreviated application is submitted under an approved petition under § 314.93, such information about the different route of administration, dosage form, or strength that FDA may require.

(7) *Bioequivalence.* (i) Information that shows that the drug product is bioequivalent to the reference listed drug upon which the applicant relies; or

(ii) If the abbreviated new drug application is submitted under a petition approved under § 314.93, the results of any bioavailability of bioequivalence testing required by the agency, or any other information required by the agency to show that the active ingredients of the proposed drug product are of the same pharmacological or therapeutic class as those in the reference listed drug and that the proposed drug product can be expected to have the same therapeutic effect as the reference listed drug. If the proposed drug product contains a different active ingredient than the reference listed drug, FDA will consider the proposed drug product to have the same therapeutic effect as the reference listed drug if the applicant provides information demonstrating that:

(A) There is an adequate scientific basis for determining that substitution of the specific proposed dose of the different active ingredient for the dose of the

member of the same pharmacological or therapeutic class in the reference listed drug will yield a resulting drug product whose safety and effectiveness have not been adversely affected.

(B) The unchanged active ingredients in the proposed drug product are bioequivalent to those in the reference listed drug.

(C) The different active ingredient in the proposed drug product is bioequivalent to an approved dosage form containing that ingredient and approved for the same indication as the proposed drug product or is bioequivalent to a drug product offered for that indication which does not meet the definition of "new drug" under section 201(p) of the act.

(iii) For each in vivo bioequivalence study contained in the abbreviated new drug application, a description of the analytical and statistical methods used in each study and a statement with respect to each study that it either was conducted in compliance with the institutional review board regulations in part 56 of this chapter, or was not subject to the regulations under § 56.104 or § 56.105 of this chapter and that each study was conducted in compliance with the informed consent regulations in part 50 of this chapter.

(8) *Labeling* -- (i) *Listed drug labeling*. A copy of the currently approved labeling for the listed drug referred to in the abbreviated new drug application, if the abbreviated new drug application relies on a reference listed drug.

(ii) *Proposed labeling.* Copies of the label and all labeling for the drug product (4 copies of draft labeling or 12 copies of final printed labeling).

(iii) A statement that the applicant's proposed labeling is the same as the labeling of the reference listed drug except for differences annotated and explained under paragraph (a)(8)(iv) of this section.

(iv) A side-by-side comparison of the applicant's proposed labeling with the approved labeling for the reference listed drug with all differences annotated and explained. Labeling (including the container label and package insert) proposed for the drug product must be the same as the labeling approved for the reference listed drug, except for changes required because of differences approved under a petition filed under § 314.93 or because the drug product and the reference listed drug are produced or distributed by different manufacturers. Such differences between the applicant's proposed labeling and labeling approved for the reference listed drug may include differences in expiration date, formulation, bioavailability, or pharmacokinetics, labeling revisions made to comply with current FDA labeling guidelines or other guidance, or omission of an indication or other aspect of labeling protected by patent or accorded exclusivity under section 505(j)(4)(D) of the act.

(9) *Chemistry, manufacturing, and controls.* (i) The information required under § 314.50(d)(1), except that § 314.50(d)(1)(ii)(c) shall contain the proposed or actual master production record, including a description of the

equipment, to be used for the manufacture of a commercial lot of the drug product.

(ii) *Inactive ingredients.* Unless otherwise stated in paragraphs (a)(9)(iii) through (a)(9)(v) of this section, an applicant shall identify and characterize the inactive ingredients in the proposed drug product and provide information demonstrating that such inactive ingredients do not affect the safety of the proposed drug product.

(iii) *Inactive ingredient changes permitted in drug products intended for parenteral use.* Generally, a drug product intended for parenteral use shall contain the same inactive ingredients and in the same concentration as the reference listed drug identified by the applicant under paragraph (a)(3) of this section. However, an applicant may seek approval of a drug product that differs from the reference listed drug in preservative, buffer, or antioxidant provided that the applicant identifies and characterizes the differences and provides information demonstrating that the differences do not affect the safety of the proposed drug product.

(iv) *Inactive ingredient changes permitted in drug products intended for ophthalmic or otic use.* Generally, a drug product intended for ophthalmic or otic use shall contain the same inactive ingredients and in the same concentration as the reference listed drug identified by the applicant under paragraph (a)(3) of this section. However, an applicant may seek approval of a drug product that differs from the reference listed drug in preservative, buffer, substance to adjust tonicity, or thickening agent

provided that the applicant identifies and characterizes the differences and provides information demonstrating that the differences do not affect the safety of the proposed drug product, except that, in a product intended for ophthalmic use, an applicant may not change a buffer or substance to adjust tonicity for the purpose of claiming a therapeutic advantage over or difference from the listed drug, e.g., by using a balanced salt solution as a diluent as opposed to an isotonic saline solution, or by making a significant change in the pH or other change that may raise questions of irritability.

(v) *Inactive ingredient changes permitted in drug products intended for topical use.* Generally, a drug product intended for topical use shall contain the same inactive ingredients as the reference listed drug identified by the applicant under paragraph (a)(3) of this section. However, an applicant may seek approval of a drug product that differs from the reference listed drug provided that the applicant identifies and characterizes the differences and provides information demonstrating that the differences do not affect the safety of the proposed drug product.

(10) *Samples.* The information required under § 314.50(e)(1) and (e)(2)(i). Samples need not be submitted until requested by FDA.

(11) *Other.* The information required under § 314.50(g).

(12) *Patent certification -- (i) Patents claiming drug, drug product, or method of use*. (A) Except as provided in paragraph (a)(12)(iv) of this section, a certification with respect to each patent issued by the United States Patent and Trademark Office that, in the opinion of the applicant and to the best of its knowledge, claims the reference listed drug or that claims a use of such listed drug for which the applicant is seeking approval under section 505(j) of the act and for which information is required to be filed under section 505(b) and (c) of the act and § 314.53. For each such patent, the applicant shall provide the patent number and certify, in its opinion and to the best of its knowledge, one of the following circumstances:

(1) That the patent information has not been submitted to FDA. The applicant shall entitle such a certification "Paragraph I Certification";

(2) That the patent has expired. The applicant shall entitle such a certification "Paragraph II Certification";

(3) The date on which the patent will expire. The applicant shall entitle such a certification "Paragraph III Certification"; or

(4) That the patent is invalid, unenforceable, or will not be infringed by the manufacture, use, or sale of the drug product for which the abbreviated application is submitted. The applicant shall entitle such a certification "Paragraph IV Certification". This certification shall be submitted in the following form:

I, *(name of applicant)*, certify that Patent No. ___ *(is invalid, unenforceable, or will not be infringed by the manufacture, use, or sale of) (name of proposed drug product)* for which this application is submitted.

The certification shall be accompanied by a statement that the applicant will comply with the requirements under § 314.95(a) with respect to providing a notice to each owner of the patent or their representatives and to the holder of the approved application for the listed drug, and with the requirements under § 314.95(c) with respect to the content of the notice.

(B) If the abbreviated new drug application refers to a listed drug that is itself a licensed generic product of a patented drug first approved under section 505(b) of the act, the appropriate patent certification under paragraph (a)(12)(i) of this section with respect to each patent that claims the first-approved patented drug or that claims a use for such drug.

(ii) *No relevant patents.* If, in the opinion of the applicant and to the best of its knowledge, there are no patents described in paragraph (a)(12)(i) of this section, a certification in the following form:

In the opinion and to the best knowledge of *(name of applicant)*, there are no patents that claim the listed drug referred to in this application or that claim a use of the listed drug.

(iii) *Method of use patent.* (A) If patent information is submitted under section 505(b) or (c) of the act and § 314.53 for a patent claiming a method of using the listed drug, and the labeling for the drug product for which the applicant is seeking approval does not include any indications that are covered by the use patent, a statement explaining that the method of use patent does not claim any of the proposed indications.

(B) If the labeling of the drug product for which the applicant is seeking approval includes an indication that, according to the patent information submitted under section 505(b) or (c) of the act and § 314.53 or in the opinion of the applicant, is claimed by a use patent, an applicable certification under paragraph (a)(12)(i) of this section.

(iv) *Method of manufacturing patent.* An applicant is not required to make a certification with respect to any patent that claims only a method of manufacturing the listed drug.

(v) *Licensing agreements.* If the abbreviated new drug application is for a drug or method of using a drug claimed by a patent and the applicant has a licensing agreement with the patent owner, a certification under paragraph (a)(12)(i)(A)(4) of this section ("Paragraph IV Certification") as to that patent and a statement that it has been granted a patent license.

(vi) *Late submission of patent information.* If a patent on the listed drug is issued and the holder of the approved application for the listed drug does not submit the required

information on the patent within 30 days of issuance of the patent, an applicant who submitted an abbreviated new drug application for that drug that contained an appropriate patent certification before the submission of the patent information is not required to submit an amended certification. An applicant whose abbreviated new drug application is submitted after a late submission of patent information, or whose pending abbreviated application was previously submitted but did not contain an appropriate patent certification at the time of the patent submission, shall submit a certification under paragraph (a)(12)(i) of this section or a statement under paragraph (a)(12)(iii) of this section as to that patent.

(vii) *Disputed patent information.* If an applicant disputes the accuracy or relevance of patent information submitted to FDA, the applicant may seek a confirmation of the correctness of the patent information in accordance with the procedures under § 314.53(f). Unless the patent information is withdrawn or changed, the applicant shall submit an appropriate certification for each relevant patent.

(viii) *Amended certifications.* A certification submitted under paragraphs (a)(12)(i) through (a)(12)(iii) of this section may be amended at any time before the effective date of the approval of the application. However, an applicant who has submitted a paragraph IV patent certification may not change it to a paragraph III certification if a patent infringement suit has been filed against another paragraph IV applicant unless the agency has determined that no applicant is entitled to 180-day exclusivity or the patent expires before the lawsuit is

resolved or expires after the suit is resolved but before the end of the 180-day exclusivity period. If an applicant with a pending application voluntarily makes a patent certification for an untimely filed patent, the applicant may withdraw the patent certification for the untimely filed patent. An applicant shall submit an amended certification by letter or as an amendment to a pending application or by letter to an approved application. Once an amendment or letter is submitted, the application will no longer be considered to contain the prior certification.

(A) *After finding of infringement.* An applicant who has submitted a certification under paragraph (a)(12)(i)(A)(4) of this section and is sued for patent infringement within 45 days of the receipt of notice sent under § 314.95 shall amend the certification if a final judgment in the action against the applicant is entered finding the patent to be infringed. In the amended certification, the applicant shall certify under paragraph (a)(12)(i)(A)(3) of this section that the patent will expire on a specific date. Once an amendment or letter for the change has been submitted, the application will no longer be considered to be one containing a certification under paragraph (a)(12)(i)(A)(4) of this section. If a final judgment finds the patent to be invalid and infringed, an amended certification is not required.

(B) *After removal of a patent from the list.* If a patent is removed from the list, any applicant with a pending application (including a tentatively approved application with a delayed effective date) who has made a certification with respect to such patent shall amend its certification.

The applicant shall certify under paragraph (a)(12)(ii) of this section that no patents described in paragraph (a)(12)(i) of this section claim the drug or, if other relevant patents claim the drug, shall amend the certification to refer only to those relevant patents. In the amendment, the applicant shall state the reason for the change in certification (that the patent is or has been removed from the list). A patent that is the subject of a lawsuit under § 314.107(c) shall not be removed from the list until FDA determines either that no delay in effective dates of approval is required under that section as a result of the lawsuit, that the patent has expired, or that any such period of delay in effective dates of approval is ended. An applicant shall submit an amended certification. Once an amendment or letter for the change has been submitted, the application will no longer be considered to be one containing a certification under paragraph (a)(12)(i)(A)(4) of this section.

(C) *Other amendments.* (1) Except as provided in paragraphs (a)(12)(vi) and (a)(12)(viii)(C)(2) of this section, an applicant shall amend a submitted certification if, at any time before the effective date of the approval of the application, the applicant learns that the submitted certification is no longer accurate.

(2) An applicant is not required to amend a submitted certification when information on a patent on the listed drug is submitted after the effective date of approval of the abbreviated application.

(b) *Drug products subject to the Drug Efficacy Study Implementation (DESI) review.* If the abbreviated new drug application is for a duplicate of a drug product that is subject to FDA's DESI review (a review of drug products approved as safe between 1938 and 1962) or other DESI-like review and the drug product evaluated in the review is a listed drug, the applicant shall comply with the provisions of paragraph (a) of this section.

(c) *Abbreviated antibiotic application.* For applications submitted under section 507 of the act, the applicant shall submit a complete archival copy of the abbreviated application that contains the information described under § 314.50 (a)(1), (a)(3), (a)(4), and (a)(5), (b), (d)(1) and (d)(3), (e), and (g). The applicant shall state whether the submission is an abbreviated application under this section or a supplement to an abbreviated application under § 314.97.

(d) *Format of an abbreviated application.* (1) The applicant shall submit a complete archival copy of the abbreviated application as required under paragraphs (a) and (c) of this section. FDA will maintain the archival copy during the review of the application to permit individual reviewers to refer to information that is not contained in their particular technical sections of the application, to give other agency personnel access to the application for official business, and to maintain in one place a complete copy of the application. An applicant may submit all or portions of the archival copy of the abbreviated application in any form (e.g., microfiche,

optical disc, and magnetic tape) that the applicant and FDA agree is acceptable.

(2) For abbreviated new drug applications, the applicant shall submit a review copy of the abbreviated application that contains two separate sections. One section shall contain the information described under paragraphs (a)(2) through (a)(6), (a)(8), and (a)(9) of this section 505(j)(2)(A)(vii) of the act and one copy of the analytical methods and descriptive information need d by FDA's laboratories to perform tests on samples of the proposed drug product and to validate the applicant's analytical methods. The other section shall contain the information described under paragraphs (a)(3), (a)(7), and (a)(8) of this section. Each of the sections in the review copy is required to contain a copy of the application form described under § 314.50(a).

(3) For abbreviated antibiotic applications, the applicant shall submit a review copy that contains the technical sections described in § 314.50 (d)(1) and (d)(3). Each of the technical sections in the review copy is required to be separate with a copy of the application form required under § 314.50(a).

(4) The applicant may obtain from FDA sufficient folders to bind the archival, the review, and the field copies of the abbreviated application.

(5) The applicant shall submit a field copy of the abbreviated application that contains the technical section described in paragraph (a)(9) of this section, a copy of the

application form required under paragraph (a)(1) of this section, and a certification that the field copy is a true copy of the technical section described in paragraph (a)(9) of this section contained in the archival and review copies of the abbreviated application.